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A Brief Review of Deep Learning Algorithms for Alzheimer's disease Detection

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Abstract: Accurate diagnosis of Alzheimer's disease (AD) is crucial, especially in its early stages, as it enables timely intervention and preventive measures before irreversible brain damage occurs. While earlier studies have used computer-based methods for AD diagnosis, many of these methods are limited by inherent observations. Early-stage AD can be diagnosed but not predicted, as predictions are only applicable before the disease becomes manifest. Deep Learning (DL) has emerged as a promising technique for early AD diagnosis. In this review, we explore relevant literature and discuss how DL can aid researchers in diagnosing the disease in its early phases.

Key Words: Alzheimer's disease, behavioral disturbance, neuro degeneration, Magnetic Resonance Image, functional Magnetic Resonance Imaging (fMRI)

1. Introduction

Translational applications of computational neuro -scientific approaches have been proven exceptionally beneficial in comprehensive mental health trials [1]. This multidisciplinary field of study can help model the biological processes governing the healthy and diseased states of the human brain and map these processes into observable clinical presentations. In the past decade, the rapid increase in high-volume biomedical datasets (neuroimaging and related biological data), concurrent with the advances in machine learning (ML), has opened innovative opportunities for the diagnosis and prognosis of neurodegenerative and neuropsychiatric disorders [2]. From a computational perspective, this recent advancement has produced the development of tools that incorporate several patient-specific observations into predictions and improve the clinical outcomes of sick person suffering from such illnesses [3], [4]. The ultimate purpose of these neuro-scientific approaches is to enhance the initial exposure and complete the treatment plan of individuals in high risk of Alzheimer's disease (AD) and AD-related cognitive decline [5], [6]. For the reasons stated above, latest studies have focused on establishing exceptionally capable approaches that use ML systems to enhance the examination of AD. The use of automatic systems capable of differentiating pathological cases from normal cases based on their Magnetic Resonance Imaging (MRI) scans (i.e., no past hypotheses are needed) will contribute immensely to the initial diagnosis of AD [7]. In this study, we review relevant studies that examine AD and use MRI data, ML and Deep Learning (DL) techniques with various AD datasets. The rest of the study is organized as follows. Brief history of AD afterwards describes the movement from ML towards DL in the AD field. Then review of AD modules and datasets, respectively. Finally conclusion is provided.

1.1 **ALZHEIMER's disease**

In 1910, in the eighth edition of Clinical Psychiatry: A Text-book for Students and Physicians, Kraepelin discussed a special group of cases with very severe cell transformations that involve too many plaques, the death of about one-third of the cerebral cortex, replacing them with specific bursts of colored neurofibrils, and represent the most severe form of malnutrition. Kraepelin, who offered a description at a time when the clinical definition of AD was unclear [9], was the first to coin the condition as ''Alzheimer's disease''. The diagnosis of the Auguste Deter disease (the first case was introduced in 1906 by the German psychiatrist Alois Alzheimer) was somewhat ambiguous; later more than hundred years, credible descriptions for the clinical definition of AD started to surface. The descriptions of AD by Dr. Alois Alzheimer in 1907 and then by

Proskin in 1909, included senile plaques and neurofibrillary sections [10]. However, when a patient's brain was clinically studied, no significant signs of arteriosclerosis were found, yet they were believed to be part of the diagnosis of the patient. In 1998, scientists from the University of Munich Germany and the Max Planck Institute of Neurobiology in Martinsried found that certain brain segments may be affected by neurofibrillary cramps and amyloid plaques [11]. such research has since been considered the first reported case of AD; more importantly, the case meets the criteria as to how AD is defined today. In 1997, Dr. Gerber and his colleagues from the Psychiatric Department of Max Planck Institute of Neurobiology examined histological cuts from F. Johan whose brain tissues had been well preserved for over 90 years. The research was regarded the second reported case of AD. An examination of the cuts revealed numerous amyloid plaques. The above research suggests that a mutational analysis of preserved brain tissue is practicable. On the 100th anniversary of Dr. Alzheimer's historic discovery, his findings were again confirmed.

Figure 1 shows a comparison of a healthy brain and a brain affected by AD [12].

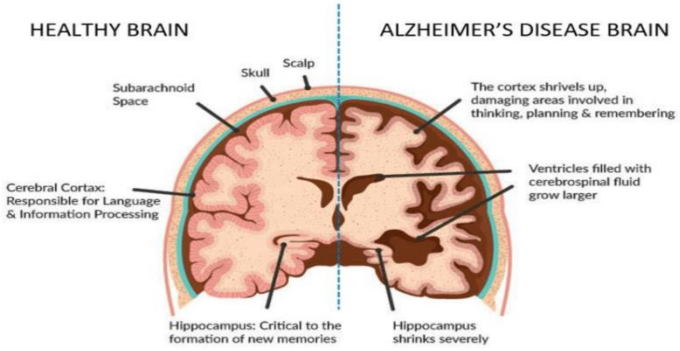

Fig 1: Comparison of a healthy brain and AD affected brain

Over the last three decades, Alzheimer's disease (AD) has climbed in the ranks of causes of death in China, moving from the 10th position in 1990 to the 5th position in 2019. Remarkably, this shift occurred despite a 0.39% decrease in the age-standardized death rate. This fact indicates that while the relative prominence of Alzheimer's disease as a cause of death has increased, the actual death rate, when adjusted for age, has slightly decreased [13]. Clearly, predicting the advancement of AD at its early stages and preventing the disease from progressing are of great importance. The identification of AD requires various medical tests and enormous multivariate heterogeneous data. However, manual comparison, visualization, and analysis of data are difficult and tedious due to the heterogeneous nature of medical tests. An efficient approach to accurately predict brain conditions is by classifying MRI scans, but this task is also challenging. However, new methodologies have been suggested to diagnosis AD at its early stages through the efficient classification of brain MRI images and the habit of label propagation with convolutional neural network (CNNs) [14]. As reported by the Alzheimer's Association in 2019, treatments for AD remain unavailable. In US alone, over five million individuals are affected by AD [15]In worldwide more than 55 million people are living with dementia, and this number is predicted to rise to 139 million by 2050 [16]. amongst them, 200,000 individuals are younger than 65 years old. The report indicates that AD is projected to disturb 10 million people, most of them in their 60s by 2050. This study states that someone is affected with AD every 67 seconds [17].

Figure 2 shows the assessment of Alzheimer's costs (in USD millions) of medicare and medicaid within the coming 50's years.

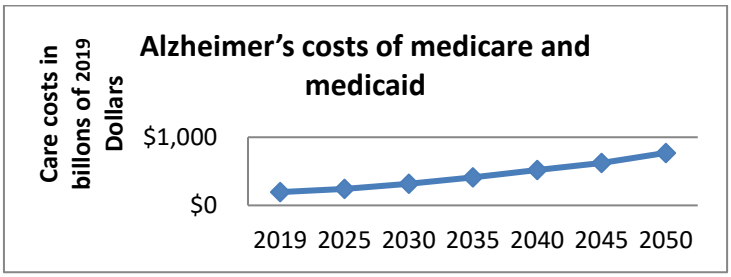

Fig 2: The Alzheimer's costs estimation.

2. Brain Imaging Techniques For Alzheimer's Disease (AD)

Brain imaging techniques widely used to non-invasively visualize the structure, function, or pharmacology of the brains [18]. The imaging techniques are usually classified into two categories: structural imaging and functional imaging [19]. Structural imaging delivers facts about the brain's structure, including neurons, synapses, glial cells, etc. Functional imaging delivers facts about the activities performed by the brain [20]. The neuroimaging techniques mostly used for AD are the following: • Magnetic Resonance Image (MRI): This imaging technique utilizes radio waves and magnetic fields to generate high-quality and high-resolution 2D and 3D images of brain structures. No harmful radiations from X-rays or radioactive tracers are generated. The most commonly used MRI for AD cases is the structural MRI, which measures brain volumes in vivo to detect brain degeneration (loss of tissue, cells, neurons, etc.). Brain degeneration is an inevitable progressive component of AD [21], [22]. Figure 3 shows an example of a structural MRI used to detect brain atrophy.

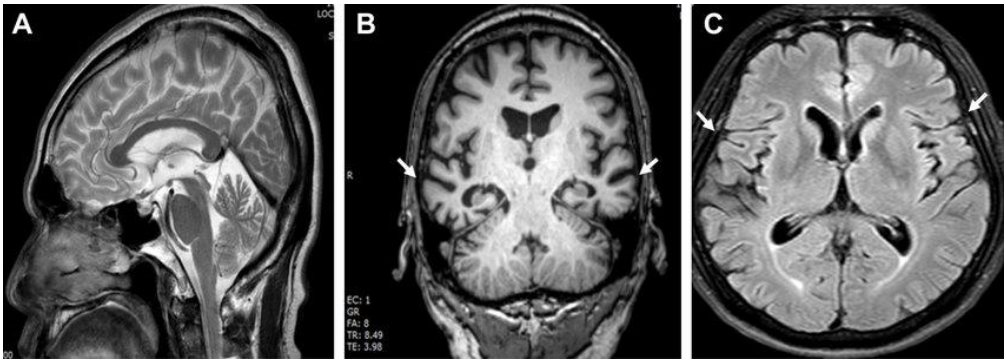

Fig 3: Structural MRI sequences. (A) T1-weighted MRI image of the patient with Alzheimer's disease with sagittal view. (B) Coronal T2WI. (C) Axial T2WI. Note: The arrows point to the hippocampal atrophy. Abbreviation: MRI, magnetic resonance imaging [24].

Alternatively, Figure 4 shows an example of functional Magnetic Resonance Imaging (fMRI), a widely used method to measure human primary visual cortex and detect brain topography.

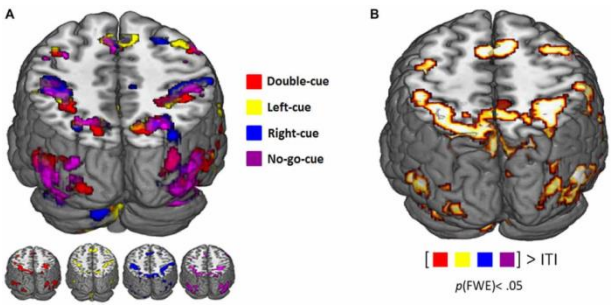

Fig 4: (A) Functional magnetic resonance imaging (fMRI) activity related to the presentation of the predictive cues (pFWE-corrected < 0.05). Color coding corresponds to the different trial types (see legend). (B) Consistent cue-evoked activation (relative to implicit inter trial interval (ITI) baseline; pFWE-corrected < 0.05) in superior

parietal lobes (SPL), dorsal premotor cortex (PMd), supplementary motor area (SMA), middle frontal gyrus (MFG), inferior [25[.

FMRI provides useful information and data about the human brain's activity, i.e., how the brain functions. fMRI methods, such as brain imaging based on arterial Blood Oxygenation Level Dependent BOLD) contrasts and spin-labeling (ASL), are sensitive to the cerebral metabolic rate of oxygen consumption and cerebral blood flow (CBF).

Figure 5 illustrates the anatomical composition of the brain and neurons. In Figure 5a, we observe a normal, healthy brain, while Figure 5b showcases a brain affected by Alzheimer's disease (AD) . Narrowing of gyri, cortical atrophy because of cholinergic neuron death, broadening of sulci, general shrinking of tissue of the brain, and swelling of ventricles that carry cerebrospinal fluid (CSF) are some of the anatomical abnormalities observed in the brains of AD patients. As AD progresses across the cerebral cortex, judgment deteriorates, which can lead to emotional outbursts and impairment of language

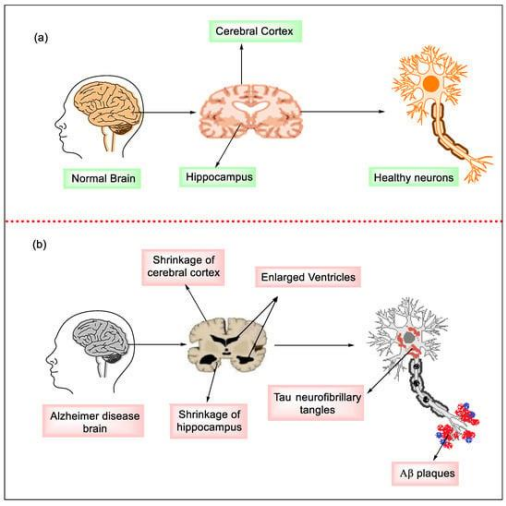

Fig 5: The physiological structure of the brain and neurons in (**a**) healthy brain and (**b**) Alzheimer's disease (AD) brain [26].

Compared to other techniques, Single-Photon Emission Computed Tomography (SPECT) is more economical than the other techniques, but it is particularly delicate for the initial examination of changes in cerebral blood flow [27]. However, this technique remains to be widely used procedures when analysing cerebral functions. Many researchers have presented that SPECT can precisely measure the cerebral perfusion of patients during AD examination. A recent study examined 116 patients suffering from AD. Amongst them, 67 individuals manifested other neurological issues, 26 individuals manifested non Alzheimer's dementia and 23 individuals were categorized as age-matched controls [28]. The study was conducted to associate and examine cerebral perfusion, cognitive proteins and cerebrospinal fluid (CSF)-tau. The subjects were divided into dementia and control case groups. The Mini-Mental State Examination, the Cambridge Cognitive Examination and a functional rating scale on symptomatic dementia were used to classify cognitive functions and functional conditions. 99mTC-HMPAO SPECT scanning was associated with CSF-tau protein levels. The selected factors enhanced the examination's precision, thus rendering the study reliable. Other previous studies focused on bilateral parietal and temporal hypoperfusion amongst AD patients, and they found significant correlations in their neuropsychological test outcomes and SPECT conclusions [29]. The authors in [29] found that SPECT is more convenient for the examination of AD compared with the CSF-tau protein.

In individuals with established Alzheimer's disease (AD), studies using ASL have consistently revealed a decrease in cerebral blood flow (CBF) in the posterior parietal region, encompassing areas such as the precuneus, posterior cingulate, angular gyrus, and superior parietal gyrus [30] The hypo metabolism pattern observed with FDG PET closely resembles that seen in ASL, and both imaging modalities exhibit comparable diagnostic capabilities. ASL's diagnostic utility remains evident even after adjusting for local gray matter

atrophy, underscoring its independent diagnostic value. However, uncorrected ASL maps may be preferred in clinical settings to enhance effect size. Figure 6 shows examples of dementia.

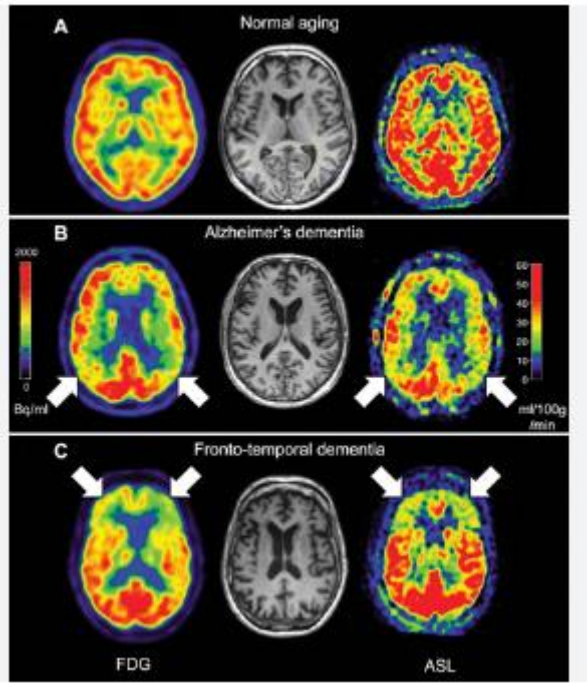

Figure 6: Examples of dementia. Transverse FDG and ASL images of, A, a healthy individual (male; age, 57 years; Mini-Mental State Examination [MMSE] score, 30), B, patient with AD (male; age, 52 years; MMSE score, 19), and, C, patient with frontotemporal lobar dementia (female; age, 53 years; MMSE score, 26). Functional images show predominant prefrontal abnormalities in FTD and parietal abnormalities in AD. Red color reflects normal metabolism and perfusion[30].

• Positron Emission Tomography (PET): This imaging procedure utilizes radiotracers, and the brain's activities are analyzed as radioactive spheres. The use of amyloid and fluorodeoxyglucose, the most commonly used tracers, for AD diagnosis is as shown in the Figure 7. Certain actions, such as looking, listening, thinking, remembering, and working, were considered [32], [33].

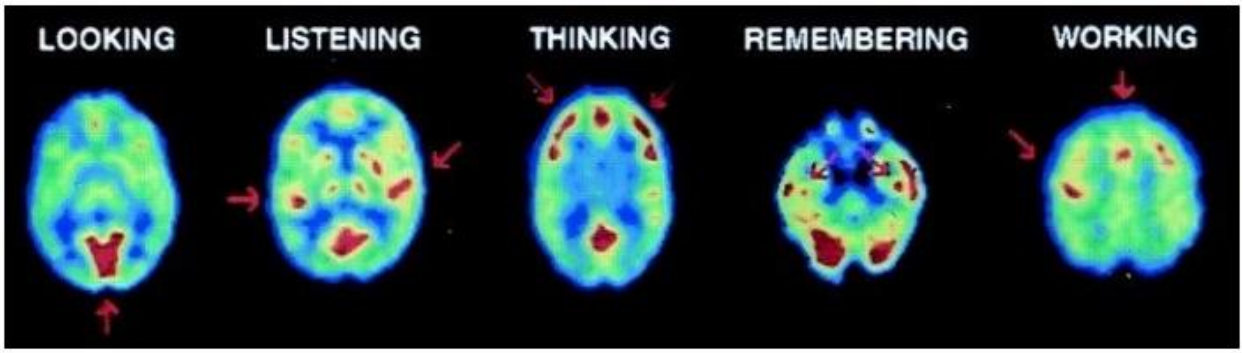

Fig 7: PET scan of a brain in normal condition [34].

Acetylcholinesterase was observed when the radioligands C-PMP and C-MP4A were utilized. This finding indicates a decrease in the temporal lobes of the AD subjects [35]. The same decline was observed amongst subjects with MCI, which eventually progressed to AD. The subjects with AD and neurodegenerative dementia were further classified. The PET ligand Pittsburgh Compound-B (PiB-C11) has been extensively studied as an amyloid imaging agent, but its clinical feasibility is limited due to its short half-life of carbon-11. Recently, florbetapir-F18 has shown in vivo correlation with post-mortem Aβ histopathology, although it has

not been directly compared with PiB-C11. In a study involving 14 cognitively normal adults and 12 Alzheimer's disease (AD) patients, both PiB-C11 and florbetapir-F18 PET scans were performed within a 28-day period. Both ligands demonstrated highly significant discrimination between the two groups and exhibited a correlation of regional uptake. These findings support the hypothesis that florbetapir-F18 can provide comparable information to PiB-C11 [36]. A temporoparietal hypoperfusion impression was detected in most of the AD subjects in PET.

False-positive results, which do not offer any value to MRI, render SPECT inconvenient for clinical purposes; by contrast, the use of neuroreceptors and FP-CIT SPECT are more useful and convenient because they enable researchers to visualize discrepancies in the nigrostriatal dopaminergic neurons.FP-CIT SPECT is an imaging procedure applied to water diffusion analysis. This method can calculate the position, direction and anisotropy of white matter in the brain. This approach focuses on the discrepancies in the microstructural architecture of water molecules [37].Although extensive exploration has been carried out to identify CSF-tau biomarker and amyloid levels, the dearth of a unanimous conclusion hinders diffusion tensor imaging (DTI) from being included as reliable method for analyzing CSF biomarkers [38].

DTI generally measures two parameters from a sMRI scan: (1) overall mean diffusivity (MD) of the water molecules and (2) fractional anisotropy (FA). DTI provides a quantitative assessment of the microscopic properties of brain tissues in vivo, utilizing metrics such as mean diffusivity (MD) and fractional anisotropy (FA).

This imaging technique is capable of identifying anomalies in brain tissue associated with conditions such as stroke, brain tumors, multiple sclerosis, and Alzheimer's disease (AD. Across various DTI studies, a consistent trend emerges, revealing higher MD and lower FA values in individuals with AD and mild cognitive impairment (MCI) when compared to age-matched control subjects) is as shown in the Figure 8 .[39].

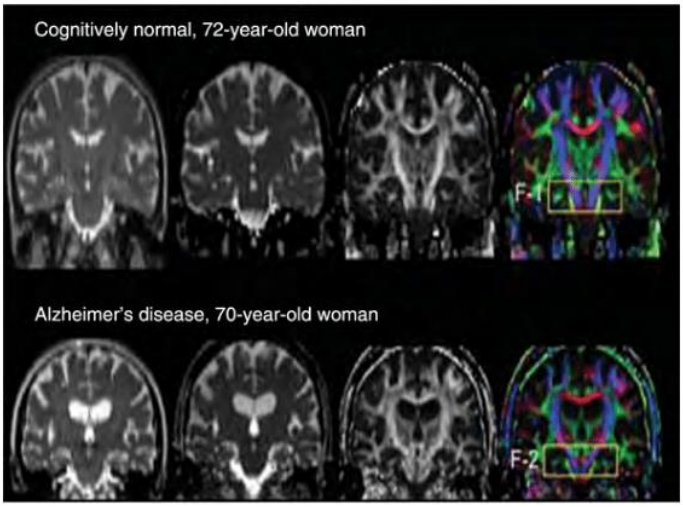

Fig 8: 3 typical diffusion tensor imaging (DTI) of the brain of an Alzheimer's disease patient compared to a cognitively normal individual. (a) Conventional MRI images of a 72-year-old cognitively normal woman and a 70-year-old Alzheimer's disease patient. (b) Mean diffusivity (MD), (c) fractional anisotropy (FA) map, and (d) color coded FA for each MRI scan. A significant difference is observed in the cingulum hippocampal area of brain (labeled F-1 on the cognitively normal image and F-2 on the Alzheimer's disease image). (Adapted from Oishi, K., Mielke, M.M., Albert, M., Lyketsos [39].

MRI biomarkers of AD: Biomarkers are regarded as the medical signs (i.e. the external manifestations of the medical statuses of patients) that can be measured precisely [40]. Biomarkers are defined in many different ways. For example, the International Program on Chemical Safety defines a biomarker as an object, architecture or a procedure for a body that can be measured and from which the existence of a disorder can be concluded [41]. AD biomarkers have the following properties: 1) Capable of identifying basic characteristics of AD's neuropathology; 2) Capable of certifying neuropath logically confirmed AD cases; 3) Efficient, capable of

identifying initial AD and capable of differentiating AD from different forms of dementias; 4) Reliable, non-invasive, easy to implement and inexpensive. Three kinds of biomarkers can help further describe AD: genetic, biochemical and neuroimaging biomarkers [42]. In the current study, MRI biomarkers are considered because of their enormous potential in AD detection. Structural images from MRI can identify atrophic modifications that influence the entorhinal cortex and the hippocampus at the initial phase of MCI, which may advance to temporal and parietal lobes in AD and affect the frontal lobes at the final phases of AD. The identification of AD and neurons that haven't experienced permanent impairment can be achieved by utilizing functional MRI and DTI. These two procedures can determine functional connectivity and structural connectivity, and they add more authority and resources to biomarkers of AD; however, they still require regulation and authorization to ensure clinical utility. These points signify that the most efficient and the most utilized MRI biomarker for AD is the structural MRI, specifically when the hippocampus volume is involved.

3. From Machine Learning To Deep Learning In AD

Over the previous decade, machine learning (ML) has played an important role in detecting MRI biomarkers for Alzheimer's disease (AD). Numerous ML methods are currently being leveraged to improve the accuracy and predictive capabilities of AD diagnosis. Alberto Benussi et al. employed a Random Forest (RF) classifier to analyze Transcranial Magnetic Stimulation (TMS) measurements collected from a multicenter cohort comprising patients with Mild Cognitive Impairment (MCI). This cohort encompassed individuals with various subtypes of MCI, including MCI due to Alzheimer's Disease (MCI-AD), MCI associated with frontotemporal dementia (MCI-FTD), MCI related to dementia with Lewy bodies (MCI-DLB), as well as a group of healthy controls (HC). At the outset of the study, all participants underwent TMS assessments, serving as the index test. These assessments were conducted in conjunction with established clinical criteria to predict the presence of different neurodegenerative disorders [43]. While ML processes have often emphasized image segmentation for bio-image classification. Hadeer A. Helaly et.al., introduced a segmentation framework called DL-AHS (Deep Learning Alzheimer's Disease Hippocampus Segmentation), designed to automate the segmentation of the left and right hippocampi for the purpose of Alzheimer's disease detection and identification[44]. Early research predominantly relied on classic texture descriptors, such as Gabor filters and Haralick texture features [45], [46].

Deep learning (DL) represents a new area of ML research that seeks to bring ML closer to its original goal of achieving artificial intelligence [47]. DL structures typically involve multiple levels of abstraction and representation to comprehend text, sound, and image data [47]. DL can be categorized into generative and discriminative architecture is as shown in the Figure 9.

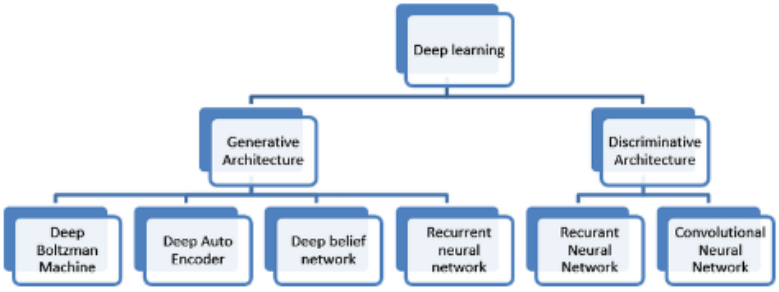

Fig 9: Categories of Deep Learning architectures.

Lawrence V. Fulton et.al., introduced convolutional blocks as a significant component of the ResNet-50 model. These networks utilize multiple filters, typically of size 3x3 pixels, to process images for classification. These filters traverse the original image using specified strides, and the learned values within these filters are multiplied with the corresponding values in the images. Subsequently, the outcomes of these filters are subjected to pooling, often involving the extraction of maximum values, effectively down sampling the data while preserving essential features. Figure 10 provides a symbolic representation of a Convolutional Neural Network (CNN).

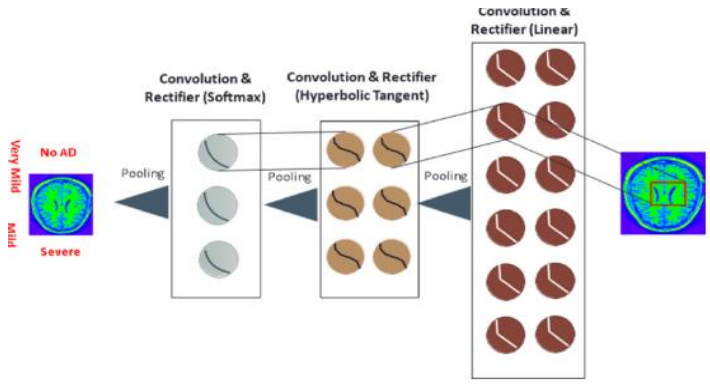

Fig 10: Example convolutional neural network for AD classification (read from right to left)[48].

The generative architecture encompasses Recurrent Neural Network (RNN), Deep Auto-Encoder (DAE), Deep Boltzmann Machine (DBM), and Deep Belief Networks (DBN). On the other hand, the discriminative design consists of Convolutional Neural Network (CNN) and RNN [47]. Modern texture descriptors for bio-image analysis, like scale-invariant feature transform and local binary patterns, have been identified by researchers [49]-[51]. These descriptors, mentioned to as handcrafted features, are manually developed to extract features from images, and they are successively served into classifiers like SVM [52]. For certain tasks, more compact and commonly used descriptors employ DL techniques, such as CNNs, to achieve the desired goals [53], [54].

However, DL applications with bio-image datasets often require extensive data, which can be challenging to obtain [57]. To address this issue, the data augmentation process is employed, which involves customizing the initial data through various transformations such as reflection, translation, rotation, brightness, saturation, and contrast adjustments [58], [41], [42]. Another commonly used method is principal component analysis (PCA) jittering, which focuses on showing the most compatible characteristics of an image by adding fundamental segments multiplied by a lesser number [59], [60]. Additionally, generative adversarial networks have been utilized to create new images that contrast with the basic ones, requiring training of a distinct network [61], [62].

DL can also be leveraged through fine-tuning pre-trained models, such as CNNs, on new datasets representing new problems. Fine-tuning allows researchers to utilize the shallowest layers of pre-trained CNNs, significantly reducing computational costs, and providing opportunities to investigate ensembles of CNNs with different parametric sets [56], [57]. Furthermore, CNNs can be employed as feature extractors and combined with various classifiers, including SVM with polynomial or linear kernels, logistic regression, random forests, and XGBoost, for efficient classification [65]. Some researchers have confirmed that classifiers using features extracted by CNNs can outperform direct application of CNNs on image data [66]. Additionally, CNNs can be useful to non-Euclidean spaces, such as patients' graphs or cortical surface images, extending their applicability beyond anatomical MRIs [57].

Deep learning-based classification methodologies are not restricted to cross-sectional anatomical MRIs, as they can also be useful to longitudinal studies, utilizing data obtained from various time points while studying the same subject [57]. Researchers have accomplished substantial achievement using SVMs to distinguish AD cases from cognitively normal cases and differentiating between stable and progressive forms of MCI [67]. For effective classification, several important characteristics, such as left and right hippocampus volume, cortical thicknesses, and other brain region metrics, have been identified [68], [69], [70], [71]. Numerous research studies have highlighted the benefits of utilizing 3D Convolutional Neural Networks (3D CNNs) to effectively capture spatial information and enhance the precision of medical image analysis such as Capsule Networks and 3D CNNs, have shown promise in detecting AD at its initial stages, achieving high accuracy rates [72 - 74].

Detecting individuals with Mild Cognitive Impairment (MCI) may serve as a viable approach for early diagnosis, potentially delaying the advancement of Alzheimer's disease and preventing irreversible brain damage [75-76].

The advancement in imaging technology from X-rays and ultrasound to computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET), represents an enhancement in our ability to observe and enrich our understanding of medical objects [77].

In conclusion, the advancement of DL in AD research has revolutionized the finding and understanding of MRI biomarkers, opening up new opportunities for precise diagnosis and prediction of the disease.

4. Modules and Data Types for Alzheimer's Disease (AD) Datasets

In this section, we will explore the various dataset modules and data types used in Alzheimer's Disease (AD) research. The primary data format utilized is neuroimaging; specifically the Neuroimaging Informatics Technology Initiative (NIfTI) file formats [78]. To handle these data, the AD dataset module is responsible for loading the scans, and it leverages the capabilities of NiBabel, a well-known Python package. The NiBabel images consist of the following components:

- Image Data Array: This is a 3D or 4D array containing the actual image data.
- Affine Array: This array provides crucial information about the image's spatial orientation and location.
- Image Metadata: This section includes descriptive information about the image.
- Uniform Dataset (UDS): The UDS compiles data from the National Institute on Aging-Funded Alzheimer’s Disease Centers, where cases undergo annual clinical examinations and neuropsychological testing. Approximately 60% of UDS cases have the apolipoprotein E genotype. Structural MRI images and data are used for the cases, with a focus on frontotemporal lobar degeneration. Researchers are actively working to enhance the UDS by incorporating various types of images and biomarkers from biospecimens, such as cerebrospinal fluid (CSF).
- Neuropathology Dataset: This dataset contains standardized neuropathology data from deceased patients who underwent autopsies.
- Minimum Dataset: Prior to the establishment of the UDS in 2005, cross-sectional data on AD cases were collected through previous research conducted at the Alzheimer ’s disease Centers.

To explore the main types of AD, we will examine datasets from prominent sources such as:

1. Alzheimer’s Disease Neuroimaging Initiative: A comprehensive initiative focusing on AD research, including the acquisition of neuroimaging and biomarker data from AD patients.
2. Harvard Medical School: Known for its contributions to AD research and the collection of valuable AD-related datasets.
3. Max Planck Institute Leipzig (Mind–Brain–Body Dataset-LEMON): A leading institution contributing to the study of AD, providing essential datasets for analysis.

By utilizing these datasets and data types, researchers can gain valuable understandings into the different types and aspects of Alzheimer's disease, furthering our understanding and potential treatments for this condition.

The ADNI dataset was sourced from more than 40 radiology hubs, encompassing a total of 509 cases, including 137 AD cases, 76 MCIc cases, 134 MCInc cases, and 162 CN cases [79]. The observation period for tracking the progression to AD was set at 18 months. ADNI has been extensively utilized in numerous studies for AD classification and understanding the transition to AD. Its primary objective is to assess whether serial MRI, PET scans, alongside other biological markers, as well as clinical and neuropsychological assessments, can be integrated to predict the progression of MCI and early AD.

The ADNI dataset was constructed based on T1-weighted structural MRIs acquired at 1.5T in compliance with the ADNI acquisition protocol. Standard patient data was meticulously examined, and additional preprocessing steps were applied, which included image reorientation, cropping, skull stripping, image normalization to the Montreal Neurological Institute standard space (MNI152 T1, 1 mm brain template), and tissue segmentation to generate probability maps for grey and white matter. The dimensions of the MRI volumes were 121 × 145 × 121 voxels. These volumes served as input for machine learning systems to perform classification tasks, such as discriminating between AD and CN, MCIc and CN, and MCIc and MCInc. The

classifier's performances on the grey matter tissue probability maps were compared with those on the white matter and whole-brain volume maps. A twentyfold cross-validation approach was employed for validation.

The MRI dataset within ADNI consisted of 260 patient cases, comprising 130 AD cases and 130 CN cases. Prior to processing this dataset, the methodology of Carli et al. [80] was employed to identify AD, utilizing characteristics like voxel cluster and voxel volume in this study.

The Harvard Medical School dataset consists of T2-weighted brain MR images. The majority of the particular images in this dataset were used for analysis. All the images in this dataset have a size of 256 × 256 pixels. In total, there are 613 images, which were classified into two categories for Alzheimer's Disease (AD) research [81]:

1. Normal Category: This category includes 27 images representing normal brain scans.
2. Abnormal Category: This category comprises 513 images representing abnormal brain scans. These abnormal images cover various conditions, including cerebrovascular, neoplastic, degenerative, and inflammatory diseases.

The dataset is used for both training and validation purposes, likely for the development of machine learning models or other analysis techniques to aid in the diagnosis and understanding of AD and related conditions. Researchers can use this dataset to study the characteristics of different brain pathologies and improve the detection and classification of brain abnormalities using T2-weighted MR images.

Max Planck Institute Leipzig Mind-Brain-Body Dataset-LEMON

The Max Planck Institute Leipzig Mind-Brain-Body Dataset-LEMON was created to investigate the interactions between mind, body, and emotion during the period of 2013-2015 in Germany [82]. This dataset consists of 228 subjects, divided into two categories: young participants (N = 154, aged 25.1 ± 3.1 years, with an age range of 20-35, and 45 females) and old participants (N = 74, aged 67.6 ± 4.7 years, with an age range of 59-77, and 37 females) [82].

The dataset was collected over a two-day period, during which the subjects underwent various major processes, including:

1. MRI at 3T fMRI: Magnetic Resonance Imaging (MRI) was conducted at 3 Tesla to visualize brain structures and activity.
2. Quantitative T1 Magnetisation-Prepared Rapid Gradient Echo (MP2RAGE): This imaging technique provides high-resolution structural brain information.
3. T2-Weighted Fluid-Attenuated Inversion Recovery (FLAIR): Used to detect brain abnormalities, especially in cases of inflammation or fluid accumulation.
4. Susceptibility-Weighted Imaging (SWI) and Susceptibility Mapping (QSM): These techniques help visualize brain vasculature and iron content.
5. Diffusion-Weighted Imaging (DWI): Used to assess the diffusion of water molecules in brain tissues, providing insights into tissue microstructure.
6. 62-Channel Electroencephalogram (EEG) Experiment at Rest: EEG data recorded to study brain electrical activity during rest [83].

In addition to neuroimaging data, the dataset also includes various physiological measurements. Blood pressure, heart rate, pulse anthropometrics, blood samples, urine samples, and respiration rate were collected during all the tests. Moreover, the institute utilized standardized clinical interview guides, such as the Hamilton Depression Scale and the Borderline Symptom List, to examine psychiatric syndromes [84]. The identification of psychiatric syndromes involved six tests and 21 questionnaires.

The Max Planck Institute Leipzig Mind-Brain-Body Dataset-LEMON offers a comprehensive resource for studying the intricate relationships between the mind, brain, body, and emotions, enabling researchers to gain valuable insights into various aspects of human health and well-being.

D. The National Health and Aging Trends Study (NHATS) To express the growing number of cases, the National Institute on Aging established the National Alzheimer's Coordinating Center (NACC) in 1999, which was financed by Alzheimer's Disease Centers. The primary objective of NACC is to support research initiatives [85]. Working closely with the Alzheimer's Disease Genetics Consortium and the National Centralized Repository for Alzheimer's Disease and Related Dementias, NACC provides invaluable resources for both exploratory and explanatory research efforts.

5. Open Access Series Of Imaging Studies (OASIS)

The Open Access Series of Imaging Studies (OASIS) is a notable project spearheaded by Dr. Randy Buckner from the Howard Hughes Medical Institute. This initiative involved collaborations with the Neuroinformatics Research Group at Washington University School of Medicine and the Biomedical Informatics Research Network [86]. The primary goal was to develop comprehensive datasets for brain imaging studies.

The dataset compiled by OASIS comprised a total of 416 cases involving subjects aged between 18 to 96 years old. Additionally, it included 100 cases of issues who were older than 60 years old. These datasets have proven to be valuable resources for researchers and scientists studying various aspects of the brain, cognition, and aging.

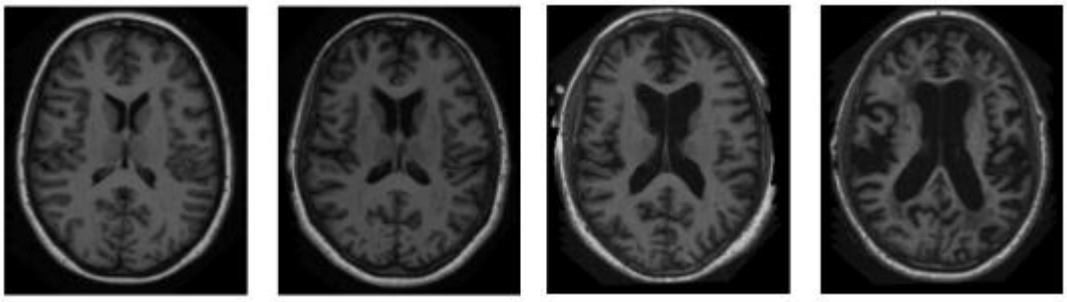

Figure 11: Sample images from OASIS dataset[87].

Figure 11 displays a sample of brain MRI images obtained from the Open Access Series of Imaging Studies dataset, further illustrating the significance of this project in advancing our understanding of the human brain and related fields.

6. **Conclusion**

In conclusion, after conducting a comprehensive literature review, we observed that the published papers in this field primarily concentrate on two main areas of research: biomarkers and neuroimaging, with a growing interest in image analysis. While the studies are considered thorough and extensive, they contribute limited knowledge to the initial detection of Alzheimer's disease (AD) since most of the selected patients are already diagnosed with AD.

This research also encompassed an examination of significant AD-related datasets, diagnostic techniques, and detection methods. Such investigations are particularly valuable for early-stage neuroimaging research. However, there remains a need for more emphasis on detecting AD in its earliest stages to enhance early intervention and potential treatment strategies.

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