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Research Article

Deep Learning Models for Early Detection of Alzheimer's Disease Using Neuroimaging Data

Md Samiun[1,*], Md Azhad Hossain[1], Professor Sanaz Tehrani[2]
[1]*Department of Business Administration, International American University, Los Angeles, CA 90010, USA*
[2]*Faculty Member of Westcliff University & International, American University, Los Angeles, CA 90010, USA*
**Corresponding Author: engineersamiun@gmail.com*

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ABSTRACT

Early identification is essential for successful intervention in Alzheimer's disease, a progressive neurodegenerative disease that is a major contributor to cognitive loss in older persons. Alzheimer's disease is difficult to detect in its early stages using conventional diagnostic techniques like neuroimaging and cognitive tests. This study investigates the use of deep learning models specifically, Convolutional Neural Networks, or CNNs to neuroimaging data to diagnose Alzheimer's disease early and the prognostic ability of Alzheimer-signature MRI biomarkers in detecting the change in cognitively normal persons into those with Alzheimer's disease (AD) dementia. Based on secondary data taken from the literature, this study assesses the performance of many deep learning architectures, such as Dense Net models, Graph Convolutional Networks (GCNs), and 3D CNNs as well as biomarkers. According to our research, CNN-based models hold great potential for precise Alzheimer's disease identification, particularly when they use three-dimensional imaging data. CNNs are the most commonly used architecture, according to a comparative study of 22 reviewed research; other models, such as GCNs and fine-tuned VGG19, exhibit noteworthy performance. The clinical applicability of such deep learning techniques and their capacity to improve patient outcomes and diagnostic precision in Alzheimer's care are also covered in this research. The study ends with suggestions for additional research, with an emphasis on addressing dataset variability limits and optimizing the model.

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1. Introduction

Alzheimer's disease (AD) is a long-term, irreversible brain illness for which there is now no effective treatment. Available medications, however, can halt its progression. Thus, the prevention and management of AD's progression depend heavily on early detection (Helaly et al., 2022). Alzheimer's disease (AD) is the most prevalent cause of dementia, accounting for 60–80% of cases (Jo et al., 2019; Singh et al., 2020). Mild cognitive impairment (MCI) is the initial symptom of AD, a neurological kind of dementia, which progressively worsens. It damages brain cells, impairs thinking and memory, and makes it difficult to complete basic tasks (Altinkaya et al., 2020; Wen et al., 2020). Consequently, AD is a neurological brain illness that progresses and has many different aspects. AD is more likely to develop in people with MCI than in others (Better, 2023; Yang et al., 2020). Since AD starts two decades or more before symptoms are noticed, people only notice its consequences after years of brain changes. According to Alzheimer's Disease International (ADI), dementia affects over 50 million individuals globally. This number is expected to rise to 152 million by 2050, meaning that one in three individuals will suffer from dementia (Helaly et al., 2022).

The biochemical process leading to AD may start over 20 years before symptoms show up (López-Cuenca et al., 2023). Amyloid peptide deposition and tau protein accumulation and phosphorylation surrounding neurons are the foundations of the current understanding of AD etiology, which results in neurodegeneration and ultimately brain atrophy (Hampel et al., 2018; Scheltens et al., 2016; Vogt et al., 2023). Age, genetic propensity (van der Lee et al., 2018), Down syndrome (Fortea et al., 2020), brain traumas (Brett et al., 2021), and cardiorespiratory fitness (Letnes et al., 2023) are among the factors linked to AD.

By 2030, the estimated yearly expense associated with dementia is likely to quadruple to $1 trillion (Adelina, 2019). The percentage of individuals afflicted by AD varies by age. In 2020, there were around 5.8 million Americans 65 and older

*Corresponding author: engineersamiun@gmail.com (Md Samiun)

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who had AD. Additionally, it is anticipated to reach 13.8 million by 2050 (Better, 2023).

The most advanced machine learning technique is deep learning. High hopes that deep learning, or artificial intelligence (AI), will revolutionize healthcare have been raised by the success of deep learning in numerous pattern recognition applications (Bhatt et al., 2021). Over the past few decades, neuroimaging has provided an intriguing non-invasive view into the human brain. Scientists from a variety of disciplines, including medical, engineering, mathematics, physics, statistics, computer science, and psychology, have been drawn to this interdisciplinary topic. In recent years, there has been a growing interest in the single-subject prediction of brain illnesses using neuroimaging. To accurately classify patients with a range of mental and neurodegenerative disorders, including schizophrenia and Alzheimer's disease, hundreds of studies have been conducted using machine learning techniques in conjunction with a variety of neuroimaging modalities, including structural, functional, and diffusion MRI (Arbabshirani et al., 2017). Non-invasively studying different parts of the human brain with previously unheard-of accuracy is now feasible because to imaging modalities like magnetic resonance imaging (MRI) and magnetoencephalography (MEG) as well as more conventional techniques like electroencephalography (EEG). The advantages of MRI-related techniques including diffusion MRI (dMRI), functional MRI (fMRI), and structural MRI (sMRI) include the provision of comprehensive functional and structural links maps as well as localized spatial data regarding the structure and function of the brain.

Numerous machine learning techniques based on high dimensional data taken from different neuroimaging biomarkers, for as brain MRI and PET, have been proposed to help with the diagnosis of AD. These machine learning techniques must not only automatically distinguish AD subjects from normal control (NC) subjects, but also forecast the likelihood that MCI subjects will progress to AD. As a result, MCI cases may be classified as either MCI converters (cMCI) or MCI non-converters (ncMCI), contingent on the risk of progression. Consequently, it is possible to naturally model the early diagnosis of AD as a multiclass classification problem (Liu et al., 2014).

Alzheimer's disease (AD) is a slowly developing illness in which pathophysiological changes that can be identified in vivo by biomarkers occur years or even decades before overt clinical symptoms appear. There are five AD biomarkers that are widely utilized in clinical trials and have been sufficiently verified to be included in clinical diagnostic criteria. Amyloid-β plaque biomarkers and tau-related neurodegeneration biomarkers are the two types of AD biomarkers that are currently available. Two of the five are analytes of cerebrospinal fluid, and three are imaging measurements (Jack & Holtzman, 2013). Cerebrospinal fluid (CSF) is currently analyzed using recognized biomarkers such as tau protein, amyloid beta protein, and phospho-tau expression levels to confirm the existence of dementia. In addition to having close association with the brain and spinal cord, CSF is recognized to function as a good source of biomarkers since it offers a comprehensive picture of the brain's diverse biochemical and metabolic characteristics (Sharma & Singh, 2016).

Researchers worldwide have unanimously determined the following criteria for a potential powerful biomarker for Alzheimer's disease (Blennow, 2005; Gu et al., 2012; Sunderland et al., 2004) those are: represent the aging of the brain, explain the pathophysiological mechanisms in the brain, any changes in pharmacology should be represented, extremely particular and delicate, results that can be replicated over time, cut-off levels that are obvious and have at least twofold changes.

Recent research has focused on employing time-to-event analysis techniques to forecast when AD dementia will progress over the follow-up period (Barnes et al., 2014). Predicting the progression of MCI individuals to AD dementia has been done using clinical and imaging-based parameters at baseline and their longitudinal change trajectory, with encouraging results. Only particular clinical measures or basic imaging characteristics, which may be less discriminative for the prognosis, have been studied (Li et al., 2019). The main objective of this research is to evaluate and compare deep-learning models for their precision and accuracy in the early detection of Alzheimer's disease and efficiency of biomarkers for early detection of Alzheimer's Disease.

2. Literature Review

Kraepelin described a unique set of cases with extremely severe cell transformations in the eighth edition of Clinical Psychiatry: A Text-book for Students and Physicians in 1910. These cases include an excessive number of plaques, the death of roughly one-third of the cerebral cortex, which is replaced by particular bursts of coloured neurofibrils, and the most severe kind of malnutrition. The term "Alzheimer's disease" was originally used by Kraepelin, who described the disorder at a period when the clinical definition was not yet apparent (Vatanabe et al., 2020).

The risk of Alzheimer's disease (AD), a neurodegenerative condition characterized by memory loss and cognitive decline, is expected to increase worldwide (Better, 2023). Since it offers chances for treatment that can delay progression, early recognition of AD is essential. The brains of those with AD and those in good health are contrasted in Fig. 1.

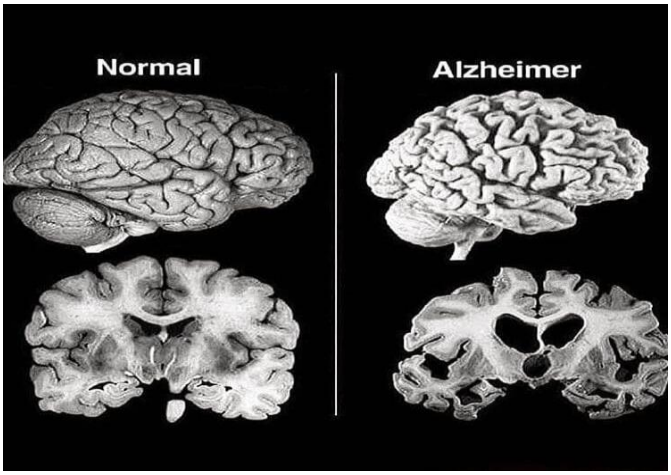

Fig. 1. Normal Brain Vs AD Brain.

In the United States, AD is currently the sixth most common cause of death. According to recent estimates, the ailment may perhaps be the third most common cause of mortality for older adults, after cancer and heart disease (Jin et al., 2019). Undoubtedly, it is crucial to anticipate AD development in its early phases and stop the disease from getting worse. Fig. 2 shows current and projected numbers of new cases of Alzheimer's disease in the US through 2050 .

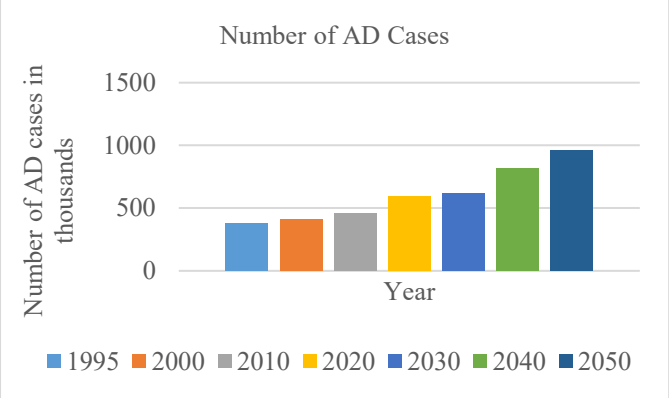

Fig. 2. Current and projected numbers of new cases of Alzheimer's disease in the US through 2050 (Hebert et al., 2001).

The financial impact of Alzheimer's disease is predicted to rise in line with the disease's anticipated rise in prevalence. The National Institute of Aging and the Alzheimer's Association (2003) estimated that the present direct and indirect expenses of providing for the 4.5 million Americans who have Alzheimer's disease are roughly $100 billion annually, demonstrating the already significant financial toll that Alzheimer's illness imposes on society. The Alzheimer's Association commissioned a study that predicted Medicare payments for people with Alzheimer's disease will rise by 75% from $91 billion in 2005 to $160 billion in the year 2010. Medicaid spending for residential dementia care was also estimated to be $21 billion in 2005, projected to rise by 14% to $24 billion in 2010 (Lives, 2004). The estimated expenditures of Alzheimer's disease for Medicare and Medicaid in the upcoming 50s are displayed in Fig. 2 (in USD millions). Fig. 3 shows the projected expenditures of Alzheimer's disease for Medicare and Medicaid through 2050 .

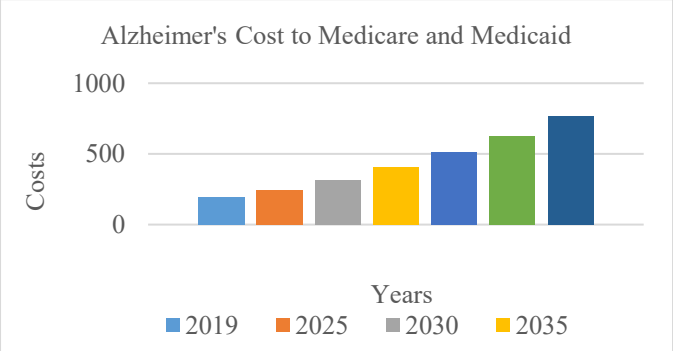

Fig. 3. The projected expenditures of Alzheimer's disease for Medicare and Medicaid through 2050 (Al-Shoukry et al., 2020).

Neuroimaging especially positron emission tomography (PET) and magnetic resonance imaging (MRI) has become crucial to detecting the structural and functional alterations in the brain linked to AD. Tau deposition and cognitive deficiencies are linked to brain atrophy, as shown by high-resolution MRI, which is a reliable indicator of Alzheimer's disease (AD) and its advancement (Frisoni et al., 2010).

A subset of machine learning called deep learning has demonstrated great promise in analyzing medical pictures because of its capacity to handle vast volumes of data and identify intricate patterns (LeCun, Bengio, & Hinton, 2015). Numerous deep learning architectures, each with distinct advantages, have been used. Because they can automatically extract important features from 2D MRI scans and achieve remarkable classification accuracy across a variety of AD diagnostic categories, Convolutional Neural Networks (CNNs) have been used extensively. However, especially for volumetric brain data, traditional CNNs may not be able to fully capture the three-dimensional spatial correlations present in MRI scans (Payan & Montana, 2015; Sarraf & Tofighi, 2016). 3D Convolutional Neural Networks (3D-CNNs) have been developed to solve this problem. By examining volumetric data and capturing the complex spatial interactions across three dimensions, these models go beyond conventional CNN frameworks and increase classification accuracy for binary and multi-class classifications (Hosseini-Asl et al., 2016; Korolev et al., 2017).

A deep learning model utilizing fluorine-18 fluorodeoxyglucose (18F-FDG) PET imaging showed encouraging results in the early prediction of Alzheimer's disease in the study by (Ding et al., 2019). The algorithm successfully identified patients an average of 75.8 months before a final diagnosis, with an 82% specificity and 100% sensitivity. This method demonstrates how PET imaging and deep learning algorithms can improve the accuracy of early diagnoses, which could lead to better patient outcomes by facilitating earlier interventions. Recent developments in computer-aided detection of mild cognitive impairment (MCI), the precursor to Alzheimer's disease (AD), have showed promise in improving diagnostic precision. Conventional techniques mostly depend on simple low-level characteristics, like mean signal intensities from PET imaging or gray matter volumes from MRI. To capture more intricate latent patterns, such as non-linear patterns, that are hidden within these low-level characteristics, Suk and Shen (2013) paper suggests an unusual deep learning-based method that makes use of a stacked autoencoder.

Even with deep learning models' achievements, there are still issues, like the possibility of overfitting because of the small dataset size and the high processing overhead (Arbabshirani et al., 2017). The lack of interpretability in these frequently over-parameterized and extremely complicated data-driven models is a major obstacle when using deep learning in AD research. Numerous studies have made an effort to enhance interpretability from various angles. Simple techniques, such as correlation analysis and grouping of neural network features or predictions, can accomplish basic interpretation (Zhou et al., 2023). Lin et al. (2019) confirmed the association between

APOE-e4 and brain aging by examining the link between prediction error and individual attributes. Ding et al. (2019) validated the model's comprehension of AD disease stages by performing t-distributed stochastic neighbor embedding (t-SNE) on neural network-generated features. Here table 1 shows the strengths and limitations of several deep learning models used in AD detection, sourced from (Razzak et al., 2018).

Table 1. Summarization of different deep learning models.

Models	Strength		Limitation
AE	Able to depict intricate and highly nonlinear patterns, excellent for reducing dimensions, simple to put into practice, CNN initialization is good.		learns to record as much data as possible instead of as much pertinent data.
RBM	able to pick up excellent generating models, able to identify trends in the absence of data		costly to compute during the training phase
DNN	Excellent for vector-based issues, able to manage datasets with a high sample count, able to identify intricate nonlinear interactions		Not ideal for images and has a sluggish training procedure, has problems with generalization
DPN	Capable of efficiently acquiring feature representation from tiny samples		performs poorly because the acquired hierarchical features from various levels are simply concatenated.
RNN	Excellent for successive two-dimensional images, ideal for long-term research		has problems with the training process because of gradients that disappear or explode.
CNN	2D	Excellent local feature performance extraction from pictures, simple to train	Incapable of encoding the three-dimensional images' spatial information
	3D	Excellent results when extracting local features from photos, able to record 3D data from a brain scan's 3D volume	costly to compute during the training phase

By using a variety of deep learning models CNN, 3D-CNN, Multiscale Deep Convolutional Networks, and GCN on a standardized dataset obtained from (Helaly et al., 2022), this study seeks to close these gaps. We want to determine the best strategy for early AD detection and offer insights into the clinical application of these cutting-edge approaches by comparing these models under comparable circumstances.

In light of earlier studies, three biomarkers for the diagnosis of Alzheimer's disease have been developed globally and published [Table/Fig-1] [17–19]. These biomarkers, which are derived from CSF, boost the validity of diagnosis by providing results that are >95% sensitive and >85% specific 20–23. Table 2 shows established biomarkers for Alzheimer's disease.

Table 2. Established biomarkers for Alzheimer's disease.

Amyloid beta	Tau protein	Phosphorylated tau
Depositions of Aβ plaque are frequently utilized to describe AD. These 42 amino acid peptides (Aβ1-42) are produced by processing amyloidogenic pathways after secretases cleave Aβ from big APP. These peptides then accumulate in the brain. AD patients' CSF analysis reveals a dramatic decrease in Aβ of approximately <500 pg/ml as compared to controls, who had 794±20 pg/ml of Aβ.	Another well-established biomarker for AD is the inclusion of the microtubule-associated protein tau in neurons. In AD patients, tau protein levels significantly increase exponentially, from around >450 to >600 pg/ml (in patients aged 51-70 years) to <300 pg/ml (in those aged 21-50 years) to nearly <500 (in those aged >71 years). Thus, it is proving to be a useful indicator for prognosis.	Tau protein is phosphorylated in over 39 different locations in AD. In contrast to controls, position 181 functions as a clear biomarker in AD. Tau protein phosphorylation causes neuronal dysfunction in addition to loss of function. Other noteworthy tau proteins that have been phosphorylated are phosphor-tau-199, -231, -235, -396, and -400.
Ref: Pérez et al. (2012)	Ref: Portelius et al. (2010)	Ref: Pérez-Grijalba et al. (2013)

3. Methodology

3.1. Comparison among Deep-learning Models

The study incorporates deep learning algorithms to categorize Alzheimer's disease (AD), mild cognitive impairment (MCI), and normal controls (NC) quantitatively. To evaluate each deep learning model's performance in this classification job, a comparison analysis was carried out, with a special emphasis on the approaches described in the seminal publication by Helaly et al. (2022), which focuses on the deep learning strategy for early Alzheimer's disease detection.

The Alzheimer's Disease Neuroimaging Initiative (ADNI) and other publicly accessible neuroimaging datasets served as the primary source of secondary data. The dataset included structural MRI scans of individuals with mild cognitive impairment (MCI), Alzheimer's disease (AD), and normal controls (NC).

22 research publications in all, each offering a different perspective on the issue, were examined and mentioned in the study. The most common method among these was Convolutional Neural Networks (CNNs), which were used in 14 studies, five of which used 3D CNNs specifically. Graph Convolutional Networks (GCNs), Multi-Convolutional Networks, CNN-El, the 3D Dense Net model, the 2D-M2IC model, the 3D-M2IC model, and a refined VGG19 model were among the other models that were investigated.

Graph Convolutional Networks (GCN) were used to comprehend the relationships between various brain regions derived from neuroimaging data, Multiscale Deep Convolutional Networks were used to improve classification performance by evaluating features at different scales, Convolutional Neural Networks (CNN) were used to extract features from MRI images, and 3D Convolutional Neural Networks (3D-CNN) were used to analyze volumetric data and capture spatial relationships. The goal of this all-encompassing strategy was to increase the categorization accuracy of Alzheimer's disease.

To preserve the subjects' privacy and confidentiality, all used data was anonymized. The study's use of medical data conformed with ethical standards. The study's step-by-step procedure is depicted in the flow chart in Fig. 4.

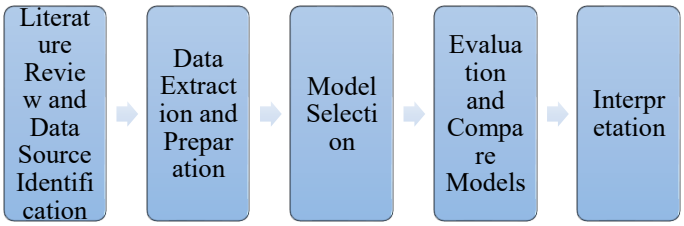

Fig. 4. Workflow.

3.2. Early Detection of AD Using Biomarkers

This study used a retrospective methodology and secondary data taken from (Dickerson et al., 2011), which demonstrated that MRI biomarkers are effective in predicting AD dementia. The investigation will concentrate on finding important MRI metrics linked to Alzheimer's disease in cognitively normal people. The findings of (Dickerson et al., 2011), which offer a comprehensive dataset comprising MRI scans, cognitive tests, and demographic data from cognitively normal individuals who were then followed for a period to track the development of AD dementia, will serve as the primary source of data for this study.

The study included a subset of cognitively normal adults who participated in the original study. The criteria for selection were: a) Adults aged 60 years and older, b) Individuals classified as cognitively normal (CN) based on baseline Mini-Mental State Examination (MMSE) scores and other neuropsychological assessments, c) Participants with a history of neurological disorders or psychiatric conditions that could confound cognitive assessment results were excluded. Analysis of variance with post hoc pairwise comparisons for continuous variables or 2 for proportions was used for group statistical comparisons (SPSS 16.0, Chicago, IL).

4. Result and Discussion

4.1. Comparative Study among Deep-learning Models

The results shown in Table 2 highlight important developments in the use of deep learning models for the categorization of AD and associated cognitive deficits. Convolutional Neural Networks (CNNs), 3D CNNs, Graph Convolutional Networks (GCNs), and Multiscale Deep Convolutional Networks are among the models that show remarkable effectiveness; many of them can distinguish between Alzheimer's patients and healthy controls with classification accuracies of over 98%. The widespread use of magnetic resonance imaging (MRI) as an imaging modality illustrates the importance of structural imaging in the evaluation of neurodegenerative diseases. Other research uses diffusion tensor imaging (DTI) and functional MRI (fMRI) to improve diagnostic precision.

Notably, Sarraf and Tofighi (2016) found that the CNN model distinguished between AD and healthy controls (HC) with an astounding 98.84% accuracy rate. Similar to this, Ge et al. (2019) found that Multiscale Deep Convolutional Networks could distinguish AD from HC with a high accuracy of 98.80%. Furthermore, the 3D CNN model created by (Basaia et al., 2019) achieved an exceptional 99.2% classification accuracy for AD versus HC. With accuracy levels of 97.11% for AD vs. NC and 96.32% for AD vs. EMCI, the 2D-M2IC Model, which was first presented by Helaly et al. (2022), likewise showed excellent performance. Finally, a multi-class accuracy of 97% was achieved by the fine-tuned VGG19 Model in differentiating between AD, EMCI, LMCI, and NC. Table 2 shows the evaluation of the accuracy of various models for Alzheimer's disease identification in Neuroimaging research.

Table 2. Evaluation of the Accuracy of Various Models for Alzheimer's Disease Identification in Neuroimaging Research

Approach	Dataset		Modality	Type of classification	Accuracy	Reference
CNN	755 in each class (AD,	ADNI	MRI	Binary, multi	AD vs. EMC vs. HC: 89.47% AD vs. HC: 95.39% AD vs. MCI: 86.84%	Payan and Montana (2015)

	MCI, and HC)				HC vs. MCI: 92.11%	
CNN	302 subjects (211 AD, 91 NC)	ADNI	MRI, fMRI	Binary	AD vs. HC: 98.84%	Sarraf and Tofighi (2016)
3D-CNN	210 subjects (70 AD, 70 NC, 70 MCI)	CAD-dementia	MRI	Binary, multi	AD vs. EMC vs. HC: 89.1% AD + MCI/NC: 90.3% AD/NC: 97.6% AD/MCI: 95% MCI/NC: 90.8%	Hosseini-Asl et al. (2016)
3D-CNN	50 AD, 43 LMCI, 77 EMCI, 61 NC	ADNI	MRI	Binary	AD vs. NC: 80% AD vs. EMCI: 63% AD vs. LMCI: 59% LMCI vs. NC: 61% LMCI vs. EMCI: 52% EMCI vs. NC: 56%	Korolev et al. (2017)
CNN	98 AD, 98 NC	Local hospitals, OASIS	MRI	Binary	AD/NC: 97.65%	Wang et al. (2018)
3D-CNN	53 AD, 228 MCI, 250 NC	ADNI	sMRI and DTI		AD/MCI/NC: 68.9% AD/NC: 93.3% AD/MCI: 86.7% MCI/ NC: 73.3%	Khvostikov et al. (2018)
3D-CNN	530 subjects (185 AD, 185 MCI, 160 HC)	ADNI	MRI	Multi	AD/MCI/NC: 88.31%	Sahumbaiev et al. (2018)
CNN	AD 192, 184 NC	ADNI	MRI	Binary	AD/NC: 99%	Spasov et al. (2018)
CNN	35 AD, 30 aMCI, 40 NC	Beijing Xuanwu Hospital	DTI, fMRI	Multi	AD/aMCI/NC: 92.06%	Wang et al. (2018)
CNN	28 AD, 28 NC	OASIS	MRI	Binary	AD/NC: 98.51%	Khagi et al. (2019)
CNN	150 subjects (AD 50, NC 50, MCI 50)	ADNI	sMRI	Multi, binary	AD/MCI/NC: 95.73% AD vs CN: 99.14% AD vs MCI: 99.30% MCI vs. CN: 99.22%	Jin et al. (2019)
GCNs	AD 12, NC 12, EMCI 12, LMCI 12	ADNI	DTI	Multi	AD/EMCI/LMCI/NC: 89%	Song et al. (2019)
Multiscale deep convolutional networks	337 subjects (198 AD, 139 NC)	ADNI	MRI	Binary	AD/NC: 98.80%	Ge et al. (2019)
3D CNN	120 subjects, 30 for each class (AD, EMCI, LMCI, NC)	ADNI	4D FMRI	Multi-classification	AD/EMCI/LMCI/NC: 93%	Parmar et al. (2020)
CNN	407 HC, 418 AD, 280 c-MCI, 533 stable MCI [s-MCI	ADNI	3D MRI	Binary	AD vs. HC: 99.2%, c-MCI vs HC: 87.1%, s-MCI vs. HC: 76.1%, AD vs. c-MCI: 75.4%, AD vs. s-MCI: 85.9%, c-MCI vs. s-MCI: 75.1%	Basaia et al. (2019)
CNN-EL	787 subjects for (AD, MCI_c,	ADNI	3D MRI	Binary	AD vs. HC: 84%, MCIc vs. HC: 79%, MCIc vs. MCInc: 62%	Pan et al. (2020)

	MCI_{nc}, HC) classes					
3D DenseNets models	600 brain MRI images	ADNI	3D MRI	Multi	AD, EMCI, LMCI, NC: 66.67%	Ruiz et al. (2020)
2D-M^2IC model	300 subjects (75 AD, 75 EMCI, 75 LMCI, 75 NC) Total size = 48,000 MRI images	ADNI	2D MRI	Multi, binary	AD vs. NC: 97.11% AD vs. EMCI: 96.32% AD vs. LMCI: 96.62% LMCI vs. NC: 98.10% LMCI vs. EMCI: 95.23% EMCI vs. NC: 98.39% AD/EMCI/LMCI/NC: 93.60%	Helaly et al. (2022)
3D-M^2IC model			3D MRI	Multi, binary	AD vs. NC: 97.36% AD vs. EMCI: 97.07% AD vs. LMCI: 97.16% LMCI vs. NC: 98.05% LMCI vs. EMCI: 96.03% EMCI vs. NC: 98.47% AD/EMCI/LMCI/NC: 95.17%	
fine-tuned VGG19 model			2D MRI	Multi	AD/EMCI/LMCI/NC: 97%	

The results are consistent with earlier studies showing deep learning algorithms are becoming more and more successful at classifying neuroimaging data. The study's high accuracy rates are consistent with those of Sarraf and Tofighi (2016) and Payan and Montana (2015), who also found that CNN architectures significantly improved performance. Nonetheless, some models like the refined VGG19 reported 97% accuracy for multi-class classification, indicating that, with the right optimization, sophisticated architectures may compete with more straightforward models. This lends credence to the current discussion about whether conventional CNNs or more intricate designs are more effective at analyzing medical images.

These findings have significant ramifications for Alzheimer's disease detection research and clinical practice. For early detection and treatment, which can drastically change the course of the disease and management approaches, high accuracy in distinguishing among AD, MCI, and NC is essential. Additionally, the capacity to accurately categorize these stages with neuroimaging can help with patient classification for clinical research and customized treatment plans.

In conclusion, there is a lot of promise for correctly categorizing Alzheimer's disease phases from neuroimaging data through the use of methods based on deep learning, especially CNNs and their derivatives.

4.2. AD Detection Using Biomarkers

There were relatively minor differences in the two samples' demographics in terms of age, gender, and educational attainment. Interestingly, compared to the CN-stable groups, the CN-AD converter groups' participants were slightly more male and older on average. All groups' educational backgrounds were similar, preventing educational disparities from confusing cognitive results.

The clinical features draw attention to the different paths taken by the CN-stable and CN-AD converter groups. All groups' baseline MMSE scores were near the ceiling, suggesting high cognitive functioning at first. Table 3 shows clinical characteristics and participants' demographics.

Table 3. Clinical Characteristics and Participant Demographics.

Characteristic	MGH		Rush	
	CN-stable (n=25)	CN-AD Converter (n=8)	CN-stable (n=25)	CN-AD Converter (n=7)
Age	71.2 (4.0)	71.5 (2.1)	76.4 (6.0)	77.7 (4.6)
Male	9 (36)	5 (63)	3 (12)	4 (57)
Education	14.9 (2.3)	14.4 (2.6)	15.6 (3.0)	15.3 (3.3)
APOE (% e4 carriers)	4 (16)	2 (25)	3 (12)	1 (14)
Baseline MMSE	29.3 (0.7)	28.9 (0.8)	29.1 (1.0)	28.0 (0.6) b
Baseline Episodic Memory	0.29 (0.7)	-0.28 (1.1) c	0.64 (0.5)	0.13 (0.5) d
Follow-up	10.4 (3.1)	11.1 (2.5)	8.3 (3.1)	7.1 (1.1)

Follow-up MMSE	29.4 (0.8)	26.0 (2.9) e	28.8 (2.1)	21.7 (2.7) e
Follow-up Episodic Memory	0.12 (0.7)	-2.3 (1.4) e	0.81 (0.5)	-1.27 (0.9) e
Source	Dickerson et al., (2011)			

Abbreviations: **AD**: Alzheimer's Disease, **CN**: Cognitively Normal, **MGH**: Massachusetts General Hospital, **MMSE**: Mini-Mental State Examination

Over a ten-year follow-up period, however, the CN-AD converters had significant drops in both their MMSE and episodic memory scores, with statistically significant decreases that indicated increasing cognitive impairment. This decrease highlights the cognitive stability of the CN-stable groups, and their scores stayed largely constant. Together with the noticeable cognitive loss in the CN-AD converters, these baseline similarities offer a useful starting point for investigating predicting biomarkers and confirming the effectiveness of deep learning models to facilitate early Alzheimer's identification.

4.2.1. Subject Group Mean (SD) Measurements of Regions of Interest (in mm)

Table 2 provides information on the mean (SD) measurements of regional cortical thickness for subjects classified as cognitively normal (CN) people who did not develop Alzheimer's disease (AD) and those who did. Cortical thickness in CN-AD converters is significantly reduced in both the Rush and MGH (Massachusetts General Hospital) samples, especially in crucial regions like the superior frontal gyrus, temporal pole, and medial temporal lobe (MTL). Statistical significance is shown at $p \leq 0.05$. These results highlight the connection between neurodegenerative processes linked to the advancement of Alzheimer's disease and cortical thinning. It's interesting to note that the main visual cortex showed varied thinning patterns, indicating that different parts of the brain are more or less vulnerable in the initial phases of AD.

Additionally, the AD-signature summary score supports the idea that particular cortical regions play a crucial role in the shift between cognitive stability to dementia by validating the thinning seen in CN-AD converters. These findings advance our knowledge of the neuroanatomical alterations linked to Alzheimer's disease and demonstrate the potential value of regional cortical thickness as a biomarker for early monitoring and detection, which would enable more focused interventions and improve diagnostic accuracy in clinical settings. Table 4 shows a region of interest measurements by topic group mean.

Table 4. Region of interest measurements by topic group mean (SD) (in mm).

Region of Interest	MGH		Rush	
	CN-stable (n=25)	CN-AD Converter (n=8)	CN-stable (n=25)	CN-AD Converter (n=7)
MTL	3.28 (0.38)	2.94 (0.43) a	3.37 (0.23)	2.83 (0.39) b
Temporal pole	3.07 (0.20)	2.77 (0.30) c	3.02 (0.29)	2.73 (0.31) a
Inferior temporal	2.48 (0.20)	2.39 (0.30)	2.89 (0.26)	2.70 (0.28)
Angular gyrus	2.48 (0.22)	2.30 (0.25) a	2.50 (0.28)	2.41 (0.23)
Supramarginal gyrus	2.54 (0.17)	2.38 (0.20) a	2.54 (0.26)	2.38 (0.13)
Superior parietal	2.17 (0.21)	2.04 (0.19)	2.05 (0.21)	2.09 (0.25)
Precuneus	2.41 (0.17)	2.25 (0.13)	2.46 (0.22)	2.38 (0.22)
Middle frontal	2.40 (0.16)	2.24 (0.11) a	2.30 (0.15)	2.20 (0.18)
Superior frontal	2.58 (0.23)	2.29 (0.19) c	2.68 (0.34)	2.40 (0.19) a
Primary visual	1.59 (0.12)	1.55 (0.08)	1.56 (0.17)	1.68 (0.25)
AD-signature summary measure	2.49 (0.14)	2.35 (0.17) a	2.65 (0.19)	2.46 (0.12) a
Source	Dickerson et al., (2011)			

Abbreviations: **AD**: Alzheimer Disease, **CN**: Cognitively Normal, **MGH**: Massachusetts General Hospital, **MTL**: Medial Temporal Lobe **Significance**: a $p<0.05$, b $p<0.001$, c $p<0.005$

5. Conclusion

A neurological condition called Alzheimer's disease (AD) causes memory loss. The need for early Alzheimer disease identification is critical because there is no approved remedy and it can't be changed. Several important findings are shown by comparing different deep learning models for the classification of Alzheimer's disease (AD), mild cognitive impairment (MCI), and normal controls (NC). First off, numerous models with accuracy rates above 90% showed that deep learning techniques, especially Convolutional Neural Networks (CNNs) and 3D Convolutional Networks (3D-CNNs), could classify neuroimaging data with significant accuracy. This demonstrates the models' potential for Alzheimer's disease early

diagnosis and detection. Crucially, these models' high classification accuracy suggests that they may be useful in clinical settings for the early detection of Alzheimer's disease, which can have a big impact on patient outcomes and treatment effectiveness.

Additionally, the study showed that the transition from cognitively normal (CN) to Alzheimer's disease (AD) dementia is linked to particular areas of cortical thinning. In comparison to the CN-stable group, both samples showed that the CN-AD converter group had notable cortical thinning in areas such the superior frontal gyrus, temporal pole, and medial temporal lobe (MTL). Furthermore, the MGH sample revealed thinning in the middle frontal gyrus and inferior parietal lobule, indicating that these areas might also play a role in the development of AD. These results emphasize how crucial it is to keep an eye on regional cortical thickness as a possible biomarker for AD early identification and treatment.

Finally, it can be suggested that the early identification and diagnosis of Alzheimer's disease (AD) and other neurodegenerative diseases may be greatly improved by combining biomarkers with deep learning algorithms.The findings highlight the need for future study to improve these models, integrate more and more varied datasets, and investigate hybrid strategies that capitalize on the advantages of various architectures. In the long run, this will help develop better diagnostic instruments for Alzheimer's disease and possibly other neurodegenerative conditions. Overall, the work highlights the potential of cutting-edge deep learning approaches to improve diagnosis accuracy and enable prompt therapies, reinforcing their important role in the classification of Alzheimer's disease.

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