



Contents lists available at ScienceDirect

Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

Review

Advancements in computer-assisted diagnosis of Alzheimer's disease: A comprehensive survey of neuroimaging methods and AI techniques for early detection

Kogilavani Shanmugavadivel^a, V.E. Sathishkumar^b, Jaehyuk Cho^{b,*}, Malliga Subramanian^a^a Department of AI, Kongu Engineering College, Perundurai, Tamilnadu, India^b Department of Software Engineering, Jeonbuk National University, Jeonju-si, Jeollabuk-do 54896, Republic of Korea

A B S T R A C T

Alzheimer's Disease (AD) is a brain disorder that causes the brain to shrink and eventually causes brain cells to die. This neurological condition progressively hampers cognitive and memory functions, along with the ability to carry out fundamental tasks over time. From the symptoms it is very difficult to detect during its early stage. It has become necessary to develop a computer assisted diagnostic models for the early AD detection. This survey work, discussed about a review of 110 published AD detection methods and techniques from the year 2011 to till-date. This study lies in its comprehensive exploration of AD detection methods using a range of artificial intelligence (AI) techniques and neuroimaging modalities. By collecting and analysing 50 papers related to AD diagnosis datasets, the study provides a comprehensive understanding of the diversity of input types, subjects, and classes used in AD research. Summarizing 60 papers on methodologies gives researchers a succinct overview of various approaches that contribute to enhancing detection accuracy. From the review, data are acquired and pre-processed form multiple modalities of neuroimaging. This paper mainly focused on review of different datasets used, various feature extraction methods, parameters used in neuro images. To diagnosis the Alzheimer's disease, the existing methods utilized three most common artificial intelligence techniques such as machine learning, deep learning, and transfer learning. We conclude this survey work by providing future perspectives for AD diagnosis at early stage.

1. Introduction

In this study, it's aims to provide a comprehensive analysis of Alzheimer's Disease progression, introduce the concept of AI and its techniques, explore their applications in healthcare, and discuss the potential for AI to contribute to early AD diagnosis and improved treatment strategies. In the early 20th century, German psychiatrist and neurologist Alois Alzheimer made groundbreaking observations of a patient exhibiting profound memory loss, language difficulties, and behavioural changes. After the patient's death, Alzheimer examined the brain and discovered unusual protein deposits, now known as plaques and tangles, which became hallmark characteristics of the disease.

AD is an irreversible, progressive brain condition that gradually reduces memory, thinking, and, ultimately, the capacity to perform even the most basic tasks. Dementia is not a typical aspect of aging, despite the fact that it becomes more common as individuals age. Alzheimer's Disease stands as the primary contributor to dementia cases among the elderly population. It typically manifests as Late-onset Alzheimer's, with symptoms emerging around the mid-60s. While Early-onset Alzheimer's, a rarity, presents symptoms from a person's 30s to their mid-60s. The brain's loss of links between nerve cells, or neurons, is another

characteristic.

Neurons carry signals from the brain to the body's muscles and functions as well as between the regions of the brain. The hippocampus and entorhinal cortex, which are important in remembering, are among the numerous brain regions that are affected by this damage before it first affects regions of the cerebral cortex that are involved in language, reasoning, and social behaviour. Over time, Alzheimer's disease gradually grows worse. People who have this illness go through various stages and at varying speeds. The person's capacity will continue to deteriorate throughout the course of the disease unless an effective therapy for the disease itself is discovered. Symptoms may worsen and then improve.

AD symptoms can manifest differently from person to person, some individuals might experience memory lapses, while others could encounter language difficulties, changes in behaviour, or problems with spatial orientation. Mild Cognitive Impairment (MCI) is a condition where individuals have memory issues than is not normal for their age but can still function normally in day-to-day activities. To determine if someone has MCI, a doctor may perform tests for thinking, memory, and language. Alzheimer's Disease is more likely to occur in people with MCI.

* Corresponding author.

E-mail address: chojh@jbnu.ac.kr (J. Cho).<https://doi.org/10.1016/j.arr.2023.102072>

Received 27 June 2023; Received in revised form 5 September 2023; Accepted 10 September 2023

Available online 13 September 2023

1568-1637/© 2023 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Early AD diagnosis offers the potential for timely interventions, tailored treatments, and enhanced patient care, thereby potentially slowing the progression of the disease and improving the overall quality of life for affected individuals. Highlighting the pivotal significance of early detection in the context of Alzheimer's dementia is imperative, as it directly influences treatment outcomes and the overall quality of life for individuals. Detecting the disease at its nascent stages empowers healthcare professionals to initiate interventions promptly, potentially slowing down its progression.

This proactive approach not only allows for the implementation of appropriate therapies but also enables patients and their families to proactively plan and manage care strategies. Furthermore, early detection opens avenues for exploring a broader spectrum of treatment options, potentially leading to more positive and enduring results. Ultimately, underscoring the vital role of early detection underscores the potential to alleviate suffering, prolong independence, and significantly enhance the well-being of those grappling with Alzheimer's dementia.

While previous research has contributed to our understanding of Alzheimer's Disease, conventional diagnostic methods often face limitations in accurately identifying the disease at its early stages due to the complexity and variability of symptoms. This deficiency has prompted the exploration of innovative AI-based approaches, which have the potential to provide more sensitive and reliable early detection methods.

Artificial intelligence "utilises computers and machines to mimic the ability of the human mind to solve problems and make decisions". It is important to remember that AI algorithms frequently learn from data and enhance their performance over time, allowing machines to carry out jobs with increased precision and efficiency. Image recognition, language translation, and speech recognition are some of the applications of AI. Machine learning is a subset of artificial intelligence and a technique for teaching machines to learn from the past using data, recognise patterns, and make predictions based on that data, in the context of the three terms.

When it comes to deep learning (DL), is a branch of machine learning, involve uses more complicated algorithms, requires bigger quantities of training data, and has highly particular applications. Recurrent Neural Networks (RNN), Generative Adversarial Networks (GAN), and Convolutional Neural Networks (CNN) are different DL models. CNNs usually used for image classification because they can detect patterns and features in images. When applied with sequential data like text or audio, RNNs can simulate the temporal connections between the data points. Long Short-Term Memory (LSTM) networks is a kind of RNN that are used to get some of the drawbacks of vanilla RNNs, such as the vanishing or ballooning gradient problem. When creating fresh data that is like training data but not exact, such as graphics or music, neural network architectures called GAN are used.

Transfer learning (TL) is the process of using a model that was previously learned to solve a new issue. In deep learning it makes it possible to train deep neural networks, only a small amount of data. Within transfer learning, a machine leverages insights acquired from prior tasks to enhance its predictive capabilities for a given task. This approach is advantageous because it reduces the need for extensive training data, accelerates training time, and can enhance the performance of neural networks, especially in scenarios with limited data availability.

The rise of Artificial Intelligence as a transformative tool in healthcare. The exponential growth in computational power, coupled with advancements in machine learning and deep learning, offered new possibilities for analysing complex medical data, including neuroimaging scans and biomarker profiles. AI is excellent at spotting small irregularities in scans and can more accurately make diagnosis based on a patient's symptoms and vital signs. AI is also used to categorise patients, keeps track, and preserve medical records, and manage them. Because of this reality, more study is being done to better understand the causes and progress of the disease so that effective treatments can be developed. Finding means to more precisely recognise the disease's physiological symptoms and early indicators, such as through

neuroimaging, which generates images of the brain, is an essential aspect of success.

New developments in neuroimaging and related medical technology would more clearly show the unique situations of each patient, laying the groundwork for an efficient study on which to base diagnoses and treatment options. Neuroimaging refers to the use of advanced imaging methods, such as MRI (Magnetic Resonance Imaging) and PET (Positron Emission Tomography), to capture detailed image brain structure, function, and activity. These images provide valuable insights into neurological conditions and help researchers and clinicians better understand brain-related disorders.

Currently, AI-based Alzheimer's Disease detection stands at the forefront of medical research and technology. The convergence of artificial intelligence and healthcare has enabled the creation of innovative approaches to diagnose AD in its early stages. These methods encompass a spectrum of AI techniques, from machine learning to deep learning, offering a potential breakthrough in addressing the complexities of AD diagnosis. This review aims to provide an insightful analysis of the existing landscape, highlighting the strides made and challenges faced in harnessing AI's power for accurate and timely AD detection.

In essence, our review not only underscores the pivotal role of feature extraction and pre-processing in neuroimaging analysis but also illuminates novel insights that hold great promise for both seasoned researchers and practitioners in the field. By delving into the intricacies of these essential processes, we aim to equip professionals with a deeper understanding of how meticulous data refinement and feature extraction can unlock new dimensions of clarity and precision in their neuroimaging investigations.

Through these insights, we aspire to empower the neuroscientific community to approach their analyses with heightened accuracy and confidence, ultimately leading to breakthroughs that contribute to our ever-evolving comprehension of the complexities of the human brain. Current Alzheimer's disease diagnostic methods exhibit limitations in early and accurate detection, often relying on subjective assessments and symptoms that become apparent only in later stages. The advent of AI-based techniques is necessary to overcome these shortcomings by providing objective and timely diagnostic tools. This study aims to provide a comprehensive analysis of Alzheimer's Disease progression, introduce the concept of AI and its techniques, explore their applications in healthcare, and discuss the potential for AI to contribute to early AD diagnosis and improved treatment strategies.

Within the scope of this paper, we have systematically classified the various challenges into three distinct categories: dataset review, pre-processing techniques, and methodologies employed, and all these are discussed in [Section 1](#). The [Section 2](#) of the paper is dedicated to an extensive discussion on datasets. Moving forward, the [Section 3](#) delves into a comprehensive exploration of pre-processing techniques. Subsequently, in the 4th section, we thoroughly examine the methods encompassing AI, Machine Learning, and Deep Learning. Finally, the 5th section is dedicated to drawing conclusions from the study's findings and outlining potential avenues for future research and work.

2. Dataset

The value of diverse datasets lies in their capacity to offer a comprehensive understanding of intricate phenomena. Through the integration of various subjects and viewpoints, these datasets facilitate more robust and widely applicable conclusions. In the datasets under examination, the substantial count of subjects bolsters the statistical validity of analyses, culminating in outcomes that are more dependable. Moreover, the distribution of Alzheimer's Disease stages within these datasets holds critical significance. An equitable portrayal of different AD stages ensures that findings hold relevance across the AD spectrum. This inclusiveness empowers researchers to meticulously explore AD progression and its manifestations, yielding insights crucial for early identification, improved management, and potential interventions.

Alzheimer's disease datasets pose challenges due to class imbalance, potentially leading to biased models favouring the majority class. Additionally, data pre-processing complexities arise from noise and inconsistencies, impacting the accuracy of analysis. Ensuring dataset reliability is vital, requiring standardized collection methods and careful validation to enhance the credibility of research outcomes. The tabulated data encapsulates the analysis from 50 papers, Table 1 in particular showcases the study of separate datasets, each characterized by different data labels such as MCI, LMCI, EMCI, AD, and CN or HC. These datasets employ various modalities for neuroimaging, including MRI, PET, and CSF. Subject selection occurred in accordance with the authors' specific criteria and the availability of participants.

2.1. Kaggle-Sourced AD Data Analysis

Heta Acharya (AlSaeed and Omar, 2022), used dataset that are freely accessible on Kaggle repositories. This dataset includes 6400 images, each measuring size is 227×227 . This dataset contains four classes, with 896 images in the Mild Demented stage, 3200 images in the Non-demented stage, 64 images in the Moderate Demented stage and 2240 images in Very Mild Demented stage. Suriya Murugan et al (Acharya et al., 2021). used the Kaggle's MRI dataset. This data has 6400 images that are 176×208 in size. The pictures have been resized to 176×176 . The SMOTE technique is used to solve the issue of class imbalance in the dataset. After SMOTE technique each class contains 3200 images. Sunday Adeola Ajagbe (Hazarika et al., 2023) uses the publicly available Kaggle MRI image dataset. The dataset contains 6400 images that was gathered was divided into three groups: a training set with 4098 images and four classes, a testing set with 1279 images and four classes, and a validation set with 1023 images and four classes. The four classes for AD include Mild Demented (MID), Moderate Demented (MOD), Non-Demented (ND), and Very Mild Demented (VMD).

2.2. ADNI Dataset Analysis

Gunawardena (Gunawardena et al., 2017) used the information from the Alzheimer's Disease Neuroimaging Initiative (ADNI - <http://adni.loni.ucla.edu/>) database. The ADNI project was started in 2003 by the National Institute on Ageing, the National Institute of Biomedical Imaging and Bioengineering, the Food and Drug Administration, private pharmaceutical firms, and non-profit organisations. Total of 504 subjects have a clinical and cognitive assessment with 1.5 T structural MRI and three classes where 101 AD, 234 Mild Cognitive Impairment (MCI) and 169 Normal healthy (NC). Sergey Korolev (Korolev et al., 2017) also used data obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. It contains 231 images from four classes: 61 Normal Cohort (NC), 77 Early Mild Cognitive Impairment (EMCI), 43 of Late Mild Cognitive Impairment (LMCI) and 50 AD.

Yan Wang (Hon and Khan, 2017) includes three classes of 35 AD, 30 MCI, and 40 NC from Beijing. Every subject consists of fMRI data and DTI. Hong Yuan (Murugan et al., 2021) used the ADNI dataset - MRI, CSF, and PET datas. 202 subjects were collected, of which 51 AD patients, 99 MCI patients, and 52 healthy controls. Anees Abrol (Maqsood et al., 2019) used 134 subjects from the ADNI dataset with sMRI and fMRI input types. 2 subjects were eliminated during the quality control process. Totally 132 subjects with 34 CN, 36 sMCI, 24 pMCI and 88 AD. Xiaowei Zhang (Adeola Ajagbe et al., 2019) used ADNI data. Which includes 36 subjects with MCI and 24 NC. Chiyu Feng (Nigri et al., 2020a) used the ADNI dataset with 397 subjects grouped into AD, MCI and NC. Ruoxuan Cui (Spasov et al., 2018) used data from ADNI - 830 subjects.

The T1-weighted structural MR brain images including 198 AD, 403 MCI, and 229 NC. Sergi G. Costafreda (Wang et al., 2018) also used ADNI data, 1.5 T MR with total of 262 subjects – 103 subjects in MCI stage, 71 subjects in AD stage and 88 subjects in HC stage. Ruoxuan Cui (Zaabi et al., 2020) used the T1-weighted MR images acquired with 1.5 T

scanners from 811 subjects. Manhua Liu (Zhang et al., 2011) used ADNI dataset with T1-weighted MRI images of 449 participants, including 97 AD, 233 MCI, and 119 NC subjects. Zhenyu Cui (Yagis et al., 2020) used ADNI with 896 subjects. Shankar K (Abrol et al., 2019) used the data from ADNI database with 256 subjects.

2.3. Analysis of dataset from the OASIS organization

Marcia Hon (Yanga, f et al., 2011) used MRI data from the Open Access Series of Imaging Studies (OASIS), accessible (<http://www.oasisbrains.org>). The OASIS database provides longitudinal and cross-sectional data. Cross sectional data was used with 416 subjects that ages ranging from 18 to 96. Muazzam Maqsood (Zhang et al., 2015) uses dataset that is publicly accessible in the OASIS repository The dataset is a collection of brain MRI images with four classes -AD, NC, MCI and LMCI. The dataset included several sagittal, coronal, and axial cross-sectional brain MRI scans. 382 image samples from participants ranging in age between 18 and 96 were collected, representing the evolution of Alzheimer's disease at each age group. The dataset of whole images, as well as the segments of GM,WM and CSF, were used to train the model.

Marwa Zaabi (Islam and Zhang, April, 2022) worked with the Oasis dataset. This dataset makes it simple to explore and analyse MRI components. The human brain is divided into various portions, including the axial, sagittal, and coronal ones. The coronal region is the one on which work is based. They used 166 images for the learning phase (80 images with healthy brains and 86 images with AD-affected brains) and 84 images in the test phase. Yanqing Zhang (Liu, January et al., 2019) Dr. Randy Buckner prepared the OASIS dataset with support from the Biomedical Informatics Research Network (BIRN), the Neuroinformatic Research Group (NRG), and the Howard Hughes Medical Institute (HHMI) at Harvard University. Each of the 416 individuals, aged 18–96, has 3 or 4 t1-weighted sMRI scans available. In the sample, there are 100 patients with very mild to moderate AD who are above 60.

2.4. A fusion of two distinct datasets for comprehensive analysis

Duaa AlSaeed (Ieracitano et al., 2019a), used two open-access databases the Alzheimer's Disease Neuroimaging Initiative (ADNI) and Minimal Interval Resonance Imaging in Alzheimer's Disease (MIRIAD). Both the dataset has two classes AD and NC. There are 741 individuals in the ADNI dataset with 314 AD and 427 NC scans. A database of MRI brain images with public access called MIRIAD contains 708 images of which 23 normal control instances and 46 Alzheimer's patients. Each subject has numerous scans taken at intervals ranging from two weeks to two years of Alzheimer's treatments. Ruhul Amin Hazarika (Silva et al., 2019) uses the open dataset ADNI, where MPRAGE MRI data are obtained. A total of 150 participant subjects are taken for consideration when gathering data. There are three classes in this dataset: CN, MCI and AD. In earlier, it was demonstrated that as people age, their hippocampus size, and Grey Matter (GM) volume change.

Ekin Yagis (Duc et al., 2020) and Wenlu Yang (Tang et al., 2019) used ADNI dataset and OASIS dataset, the two public accessible datasets on AD. MRI scans from a subset of the ADNI 2 dataset with 100 in the AD group and the remaining 100 in the HC group. There are 416 total subjects in OASIS 1 Cross-sectional data (316 HC and 100 AD) ranging in age from 18–96. Chin-Fu Liu (Sato et al., 2019) used the ADNI 1, ADNI GO, ADNI 2, and BIOCARD databases. In ADNI data 819 subjects were selected out of 3566 T 1.5 T1 scans and in BIOCARD data 324 subjects were selected from 744 1.5 T T1 scans. Han Woong Kim (Chitradevi and Prabha, 2020) used the AD Neuroimaging Initiative (ADNI) database with 139 AD and 347 NC patients and dataset from the Nuclear Medicine Department of Severance Hospital (Seoul, South Korea) Severance data with 73 AD and 68 NC patients. Samsuddin Ahmed (Ding et al., 2019) uses both ADNI and GARD dataset. GARD dataset contains 326 subjects and in the ADNI dataset 60 subjects are used.

Table 1
Review of the Neuro Images Dataset.

Year	Author	Dataset Utilized	Number of Subjects	Input Type	Class Labels	
2022	Duaa AlSaeed (Acharya et al., 2021)	ADNI	741	MRI	NC	
2021	Heta Acharya (Murugan et al., 2021)	MIRIAD	708	MRI	AD	
		MRI images	6400		MID	
					MOD	
					VMID	
2021	SURIYA MURUGAN (Zhang et al., 2011)	MRI images	12800	MRI	ND	
					MID	
					MOD	
					VMID	
2021	Sunday Adeola Ajagbe (Zhang et al., 2015)	MRI images	6400	MRI	ND	
					Four classes	
					-MID	
					-MOD	
2023	Ruhul Amin Hazarika (Adeola Ajagbe1 et al., 2019)	ADNI	150	sMRI	-VMID	
					-ND	
					CN	
					MCI	
2017	Gunawardena (Gunawardena et al., 2017)	ADNI	504	MRI, PET	AD	
					MCI	
					NC	
					LMCI	
2017	Sergey Korolev (Korolev et al., 2017)	ADNI	231	MRI	EMCI	
					NC	
					AD	
					AD	
2017	Marcia Hon (Wang et al., 2018)	OASIS	200	MRI	AD	
					NC	
					NC	
					AD	
2020	Marwa Zaabi (Cui and Liu, 2019b)	OASIS	156	MRI	NC	
					NC	
					NC	
					NC	
2019	Muazzam Maqsood (Abrol et al., 2019)	OASIS	382	MRI	NC	
					VMID	
					MID	
					AD	
2020	Eduardo Nigri, Nivio Ziviani (Li and Liu, 2019a)	ADNI2	1248	MRI	AD	
					AIBL	NC
					ADNI1	AD
					NC	
2018	Simeon E. Spasov (Cui and Liu, 2019a)	ADNI1	376	MRI	AD	
					NC	
					NC	
					NC	
2018	Yan Wang (Costafreda et al., 2011)	ADNI	105	fMRI, DTI	NC	
					MCI	
					AD	
					AD	
2011	Hong Yuan (Liu et al., 2020b)	ADNI	202	MRI, CSF, PET	AD	
					MCI	
					NC	
					NC	
2020	Ekin Yagis (Cui et al., 2019)	ADNI	200	MRI	AD	
					OASIS	HC
					ADNI	CN,
					ADNI	sMCI,
2019	Anees Abrol (SK et al., 2019)	ADNI	134	fMRI	pMCI,	
					sMRI	AD
					sMRI	AD
					sMRI	AD
2011	Wenlu Yang (Hon and Khan, 2017)	OASIS	416	MRI	AD	
					ADNI	AD
					ADNI	ND
					ADNI	MCI
2015	Xiaowei Zhang (Maqsood 1 et al., 2019)	ADNI	50	fMRI	NC	
					NC	
					AD	
					NC	
2018	Yanqing Zhang (Zaabi et al., 2020)	OASIS	416	sMRI	AD	
					NC	
					NC	
					AD	
2019	Chin-Fu Liu (Islam and Zhang, April, 2022)	ADNI	1143	MRI	NC	
					BIOCARD	MCI
					AD	
					AD	
2018	Cosimo Ieracitano (AlSaeed and Omar, 2022)	IRCCS	189	EEG	MCI	
					AD	
					HC	
					AD	
2019	Iago R. R.Silva (Hazarika et al., 2023)	MIRIAD	69	MRI	HC	
					AD	
					AD	
					AD	
2019	Nguyen Thanh Duc (Yagis et al., 2020)	NRCD	331	rs-MRI	AD	
					NC	
					MMSE perdition	
					HC	
2019	Ziqi Tang (Yanga, f et al., 2011)	UCD-ADC Brain Bank	43	WSI (Whole Slide Image)	MCI	
					AD	
					AD	
					AD	
2019	Ryosuke Sato (Liu, January et al., 2019)	Dong -A university of Korea	380	PET	AD	
					HC	
					MCI	
					AD	

(continued on next page)

Table 1 (continued)

Year	Author	Dataset Utilized	Number of Subjects	Input Type	Class Labels
2019	Chitradevi (Kim et al.,)	Chettinad Health City, Chennai	200	MRI	AD NC
2018	Yiming Ding (Ahmed et al., 2019)	ADNI Aprivate data	1002 40	PET	AD MCI NC
2019	Silvia Basaia (Nigri et al., 2020a)	ADNI Milan dataset	1409 229	MRI	AD NC
2019	Chong-Yaw Wee (Spasov et al., 2018)	ADNI1 ADNI2 Asian cohort	1012 1083 347	MRI	AD/NC NC/EMCI NC/LMCI
2018	Mingxia Liu (Sørensen et al., 2017)	ADNI1 ADNI2 MIRIAD AIBL	1984	MRI	AD sMCI pMCI NC
2019	Bi Xiaojun (Li et al., 2019)	Beijing Easy monitor Technology	12000	EEG	AD MCI NC
2020	Han Woong Kim (Kim et al.,)	ADNI Severance	627	MRI PET	AD NC
2019	Charles K. Fishe (Ding et al., 2019)	CAMD Online Respiratory	1909	Numerical Features	ADAS-Cog, MMSE and laboratory tests
2020	Ning An (Basaia et al., 2019a)	NACC UDS	23,165	Numerical Features	AD NC
2019	Cosimo Ieracitano (Basaia et al., 2019b)	IRCCS	189	EEG	AD MCI HC
2011	Noramalina Abdullah (Liu et al., 2019)	ADNI	32	MRI	AD NC
2017	Zhe Xiao (Xiao, : et al., 2017)	ADNI		MRI fMRI PET DTI	AD NC
2019	CHIYU FENG (Li and Liu, 2019a)	ADNI	397	MRI PET	AD MCI (sMCI,pMCI) NC
2019	Ruoxuan Cui (Ieracitano et al., 2019a)	ADNI	830	MRI	AD MCI (sMCI,pMCI) NC
2011	Sergi G. Costafreda (Ieracitano et al., 2020)	ADNI	262	MRI	AD MCI HC
2016	Lauge Sørensen (Duc et al., 2020)	ADNI AIBL CADDementia	504 145 354	MRI	AD MCI NC
2019	Hongming Lia (Sato et al., 2019)	ADNI ADNI-GO&2 AIBL	1711 803 435	MRI	AD MCI (sMCI,pMCI) NC
2019	Ruoxuan Cui (Chitradevi and Prabha, 2020)	ADNI	811	MRI	AD MCI (sMCI,pMCI) NC
2019	Manhua Liu (Abdullah1 et al., 2011)	ADNI	449	MRI	AD/NC MCI/NC
2019	SAMSUDDIN AHMED (Bi and Wang, 2019)	ADNI GARD	386	MRI	AD NC
2019	Zhenyu Cui (Fisher et al., 2019)	ADNI	896	MRI	AD MCI NC
2019	Shankar K (An et al., 2020)	ADNI	287	MRI	AD MCI NC

Eduardo Nigri, Nivio Ziviani (Basaia et al., 2019a) used Disease Neuroimaging Initiative2 (ADNI) data obtains MRI scans and performs a clinical AD diagnosis every six to twelve months. The Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing3 (AIBL) is the second one, and it also gathers both kinds of data. AD and NC are the two classes used Each image is a $100\times100\times100$ of 3D tensor. Spasov (Basaia et al., 2019b) used ADNI1 dataset and comprises MRI (t1- weighted MP-RAGE images at 1.5 T with $256\times256\times256$ voxels and a target voxel size of 1 mm3), and clinical features. The 376 subjects were grouped as AD with 192 subjects and NC (Normal Controls) with 184 subjects. Lauge Sørensen (Liu et al., 2019) used ADNI, AIBL and CADDementia

datasets which are public available data.504 subjects were used in ADNI data, 145 subjects with AIBL data and 354 subjects with CADDementia data. Hongming Lia (Bi and Wang, 2019) worked with the 1711 ADNI-1 data, 803 ADNI-GO&2 data and the 435 AIBL data were used with three stages. Yiming Ding (Fisher et al., 2019) used ADNI dataset with 1002 patients and an independent test set 18 F-FDG PET imaging studies from 40 patients. Silvia Basaia (An et al., 2020) uses the ADNI MRI data acquisition protocol in ADNI and an independent dataset of 3D t1 weighted images Milan dataset. For ADNI data 1409 subjects with 294 AD, 763 MCI, and 352 HC patients. For Milan data 229 subjects with 124

AD, 50 MCI and 55 HC. Chong-Yaw Wee (Ieracitano et al., 2020) included ADNI, ADNI2 and Asian cohort datasets. In which 1083 subjects with 242 CN, 415 MCI and 355 AD from the ADNI-2 dataset and 1012 subjects with 300 CN, 314 EMCI, 208 LMCI and 261 AD from the ADNI-1 data. Subjects were primarily Caucasian and aged between 55 and 90 years old. Then 347 subjects with 176 CN, 128 MCI and 43 AD from the Asian cohort datasets.

Mingxia Liu (Abdullahi et al., 2011) used four public datasets with 984 subjects, including 1) Alzheimer's Disease Neuroimaging Initiative-1 (ADNI-1 with 181 AD, 226 NC, 165 pMCI and 225 sMCI subjects), 2) ADNI-2 (143 AD, 185 NC, 37 pMCI, and 234 sMCI subjects), 3) Minimal Interval Resonance Imaging in Alzheimer's Disease (MIRIAD with 46 AD and 23 NC subjects) and 4) Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL with 72 AD and 447 NC subject).

2.5. Utilizing multiple source datasets for AD analysis

Cosimo Ieracitano (Li and Liu, 2019a) and Cosimo Ieracitano (Cui and Liu, 2019a) used dataset of 189 EEGs with 63 AD, 63 MCI and 63 HC which was collected at IRCSS Centro Neurolesi Bonino-Pulejo of Messina (Italy). Iago R. R. Silva (Costafreda et al., 2011) used the data from MIRIAD (Minimal Interval Resonance Imaging in Alzheimer's Disease) dataset from UCL (University College London). This contains MRI images of 69 patients in which 23 were HC, and 46 were Alzheimer's Disease AD. Nguyen Thanh Duc (Sørensen et al., 2017) collected data from individuals enrolled at the Chosun University National Dementia Research Centre (Gwangju, South Korea) NRCD with 331 subjects. Ryosuke Sato (Li et al., 2019) uses 379 PET images provided by Dong-A University of Korea. The BAPL (Brain Amyloid Plaque Loading) score that includes 144 BAPL3, 48 BAPL2 and 188 BAPL1 subjects. The PET image were $400 \times 400 \times 110$ voxels of which each voxel size is $1.02 \text{ mm} \times 1.02 \text{ mm} \times 1.5 \text{ mm}$.

Chitradevi (Cui and Liu, 2019b) segments the internal brain regions,

such as the GM, WM, CC, and HC, using axial, coronal, and sagittal slices of a brain MR image from Chennai's Chettinad Health City. The 2D T2 flair weighted MRI brain scans are considered. To segment the GM and WM, the axial slice has been considered; to segment the CC, the sagittal slice has been considered; and to segment the HC, the coronal slice view has been selected. 200 images are grouped into Normal Control (NC) and AD patients AD. Noramalina Abdullah (Liu et al., 2020b) uses data from Advanced Medical and Dental Institute (AMDI) with axial T2 FLAIR-weighted data. The data contains 32 patients (22 abnormal and 10 normal) within the age of 20–40 years old.

Bi Xiaojun (Ahmed et al., 2019) collected the EEG data using Beijing Easy monitor Technology. The dataset consists of 12,000 images with 1000 images on each instance with 4 HC, 4 MCI and 4 mild-to-severe AD patients Charles K. Fische (Cui et al., 2019) extracted data from the Coalition Against Major Diseases (CAMD) Online Data Repository (CODR-AD). 1909 patients with MCI or AD are extracted. Ning An (SK et al., 2019) used the National Alzheimer's Coordinating Centre data, 165 samples from NACC UDS.

The input types of image-based potential biomarkers include Magnetic Resonance Imaging, Positron Emission Tomography, Electro Encephalo Gram, Diffusion Tensor Imaging and Cerebro-Spinal Fluid. MRI techniques show brain abnormalities related to the chance of converting to AD from MCI as well as other behavioural outcomes and patterns of brain damage that distinguish AD from other brain disorders. In amyloid PET imaging, "tracer molecules" cling to the amyloid plaques that damage brain connections and are related to Alzheimer's disease. This enables to determine whether a patient's brain contains the plaques or not.

In Fig. 1, the different input types used: (a) Diffusion Tensor Imaging (DTI) to delineate White Matter. (b) Functional Connectivity has cross sectional (axial) and longitudinal view (sagittal) (c) Brain damage pattern of Magnetic Resource Imaging (MRI) and Positron Emission Tomography (PET) images are utilized to find AD in its early stages. (d) Electro Encephalo Gram (EEG) signal acquisition. (e) Cerebro-Spinal

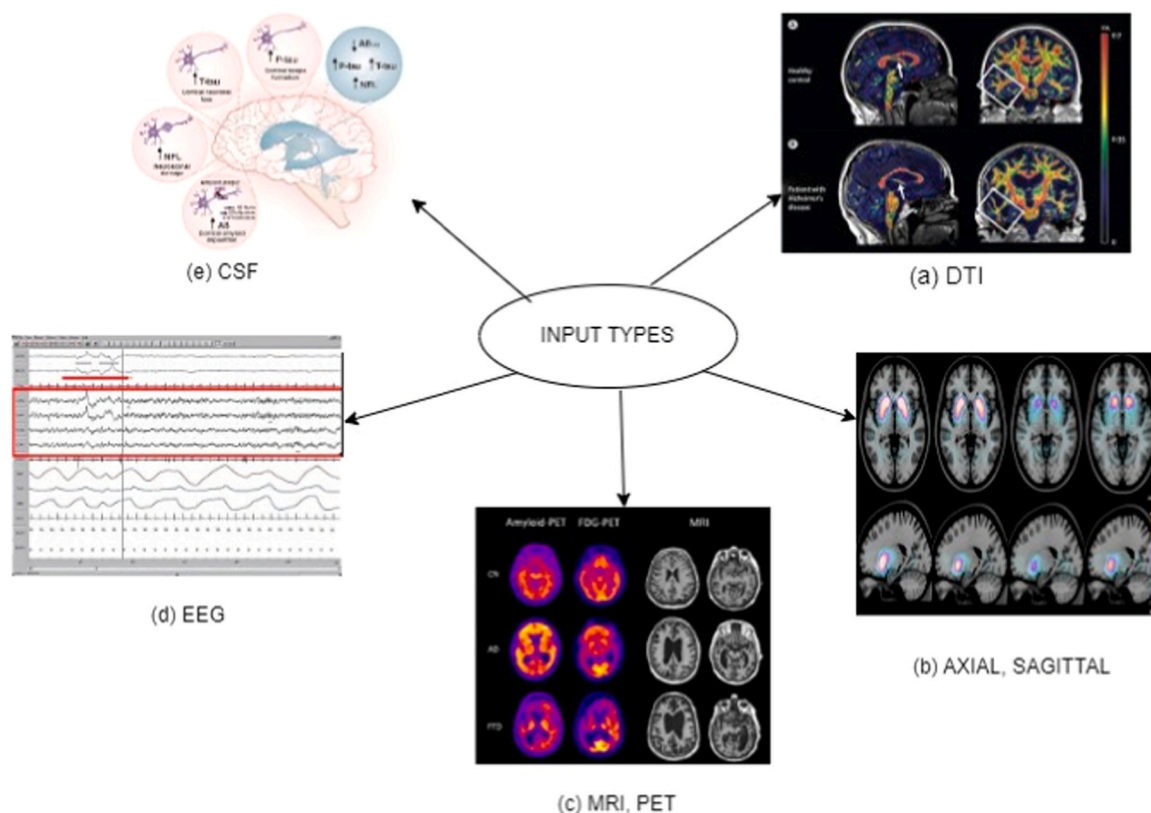


Fig. 1. A graphical representation of different input types.

Fluid (CSF) biomarkers.

White matter (WM) microstructure changes in neurological illnesses can be mapped using Diffusion Tensor Imaging (DTI). T-tau, P-tau, and A-42 are the three primary CSF biomarkers of neuro degeneration, CSF NFL, and plasma T-tau was all significantly correlated with Alzheimer's disease. Fig. 2 represents the parameters considered for different input types of neuro images.

3. Pre-processing

The transformation of raw data into information that machine learning algorithms can use is known as data pre-processing. It is challenging to directly apply machine learning models to real world data since it includes various forms of noise, incomplete data, and potentially even being presented in an unfitting format. Data pre-processing, which is necessary to clean the data and prepare it for the model, boosts the accuracy and effectiveness of ML model. Feature extraction and pre-processing stand as indispensable constituents of neuroimaging analysis. Their role in refining data quality, minimizing noise, ensuring data coherence, boosting statistical power, aiding interpretation, and refining investigative precision underscores their significance in unravelling the intricate workings of the human brain.

Table 2 offers a summary of the preprocessing methods, utilized algorithms, and the resultant achieved accuracies. The 3D MRI brain images were employed to enhance the model's effectiveness. Image processing algorithms are difficult to implement in a 3D MRI film. The 3D MRI films must be converted into a sequence of 2D images. For visually focused area, hippocampus is chosen because it is the area of the brain that is most impacted by AD. With the 2D photos, the skull-stripping (Korolev et al., 2017; Liu et al., 2020b; Cui et al., 2019) procedure is performed. A histogram-based technique (Adeola Ajagbel et al., 2019) is used to remove the skull. And it is used for matching images before registration and data winsorization (Cui and Liu, 2019a). Then, to reduce image noise to produce a less pixelated image, the MRI smoothing technique (Acharya et al., 2021; Abrol et al., 2019) is applied.

The MRI images can be smoothed using FWHM Gaussian filter (Maqsood 1 et al., 2019; Yagis et al., 2020; SK et al., 2019). High-pass temporal filtering is used for removing low level noise. After the cerebellum has been removed, structural MR images are divided into the three tissues of Grey Matter (GM), White Matter (WM), and Cerebro-Spinal Fluid (CSF) using FAST in the FSL package. While training a small dataset, over fitting in a large neural network is reduced

by data augmentation (Zaabi et al., 2020; Bi and Wang, 2019). The REST Toolkit is used to filter data with a low frequency range. To improve all the regions of the brain and increase contrast, including the CSF, GM, and WM, the adaptive histogram equalisation (Kim et al., ; Fisher et al., 2019) method has been used.

Otsu thresholding approaches (Ahmed et al., 2019) are used for skull stripping (Liu, January et al., 2019), which extracts the homogenous intensity areas and subtle transitions that exist between brain and non-brain tissue. The per-processing includes the phases of skull stripping, voxel intensity standardisation, MCFLRIT, and spatial smoothing were also used during the anatomical data pre-processing stages (Sarraf and Tofghi., April, 2021; Kim et al., ; Xiao, : et al., 2017). Some other pre-processing technique and algorithms used for diagnosing AD are given in below table with accuracy of each model. The Table 2 represent algorithms used and accuracy obtained in each model using different pre-processing techniques.

4. Artificial Intelligence Techniques

Artificial Intelligence is the term used to describe how machines simulate or resemble human intelligence. Learning, reasoning, and perception that are enhanced by computers are among the objectives of artificial intelligence. Today, artificial intelligence is applied in a variety of sectors, including banking and healthcare. Strong AI handles tasks that are more complex and human-like, whereas weak AI tends to be simple and single task-oriented. Machine Learning falls within the domain of AI, encompassing the concept that computer programs possess the ability to independently learn and accommodate novel data, without the requirement of human assistance. Through the assimilation of extensive volumes of unstructured information, like text, images, or videos, deep learning methodologies empower the achievement of independent learning.

AI algorithms are naturally more complicated. AI algorithms function by taking in training data. The key difference between different kinds of AI algorithms is in the manner in which that data is collected and labelled. Basically, an AI algorithm uses training data—labelled or unlabelled, provided by developers or gathered by the programme itself to learn and improve on itself. It then completes its jobs based on the training data. Some AI algorithms can be trained to learn on their own and use fresh data to modify and improve their workflow. Others will require a programmer's assistance to simplify. The utilization of training data within AI algorithms enhances the comprehension of the learning

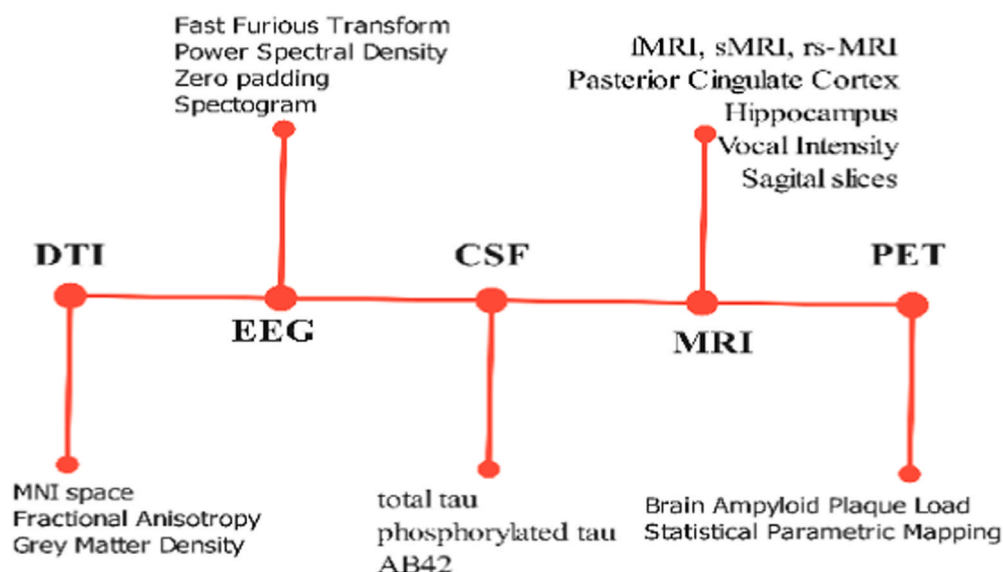


Fig. 2. Parameters used in Neuro Images.

Table 2

A review of the Pre-processing Techniques, Algorithms and Accuracy obtained.

Reference Number	Pre-processing Techniques	Algorithms Utilized	Accuracy
Machine Learning Algorithms			
(Hazarika et al., 2023)	2D axial slices Image Normalization	Random Forest SVM KNN	88 95.08 85.12
(Hon and Khan, 2017)	Alignment and spatial normalization SPM8 toolbox	PCA, SVM	i 97.8 ii 80.7
(Maqsood 1 et al., 2019)	Smoothing using a Gaussian kernel REST Toolkit	Linear Regression KNN Neural Network Classification Tree Random Forest SVM	88.25 75.50 82.25 73.50 79.0 78.55
(Liu, January et al., 2019)	Contrast enhancement using Histogram Equalization Skull stripped using Otsu's threshold	PSO, GA, CS, GWO	98
(Duc et al., 2020)	Gaussian smoothed images	SVM	73.3
(An et al., 2020)	Accentuation, Gaussian filtering ROI Extracted, Noise Removal	DT, KNN, CNN	96.23
(Basaia et al., 2019a)	Normalization	LogitBoost, Bagging, AdaBootM, Random Forest, Stacking, Vote, DELearning	80, 82, 75, 82, 63, 65, 87
(Basaia et al., 2019b)	CWT features extraction BiS features extraction	MLP	96.5
(Liu et al., 2019)	Image enhancement techniques	SVB	65
(Xiao, : et al., 2017)	Image Pre-processing Segmentation of brain tissue	SVM(RBF)	85.59
(Sørensen et al., 2017)	Spatial smoothing Anterior Commissure Posterior Commissure N3 algorithm Skull stripping	DSML	92
(Ieracitano et al., 2019b)	Normalization	Autoecondor, MLP, LR, SVM	95
Machine Learning and Deep Learning Algorithms			
(Gunawardena et al., 2017)	Image processing techniques	CNN, SVM (RBF kernel)	84.4
(Acharya et al., 2021)	Smoothing technique	CNN (ResNet) Classify -SVM, Random Forest	i 99 ii 96
(Abrol et al., 2019)	Image enhancement techniques	CNN SAM LDA	92.8 79.8 62.7
(Liu et al., 2020b)	Skull-stripping using both BSE and BET	CNN, SVM	91.8
(AlSaeed and Omar, 2022)	2-d gray scale images (PSD images)	CNN MLP -SVM LDA	83.3 59.40 56.84 55.70
(SK et al., 2019)	Smoothing using a Gaussian kernel	CNN-ResNet	91.8
(Silva et al., 2019)	N3 algorithm Skull Stripping	SVM CNN-SVM	80
(Liu et al., 2020a)	GM VBM ROI	CNN	90.56
Deep Learning and Transfer Learning Techniques			
(Murugan et al., 2021)	Image Data Generator	CNN Resnet 50	88 75

Table 2 (continued)

Reference Number	Pre-processing Techniques	Algorithms Utilized	Accuracy
Machine Learning Algorithms			
(Yagis et al., 2020)	gICA Spatial smoothing, Gaussian kernels and temporal filtering WSI	VGG16 Modified AlexNet CNN	85 95.70 85.27
(Tang et al., 2019)	Segmentation	CNN	91
(Bi and Wang, 2019)	Data augmentation Technique	CNN	90.05
(Kim et al.,)	MNI-152 based Spatial normalization	CNN	95.14
(Nigri et al., 2020a)	Statistical Parametric Mapping (SPM12)	CNN	95.24
(Adeola Ajagbe1 et al., 2019)	Histogram-based technique	Hybrid Methods LeNet, AlexNet, MobileNet v1, ResNet50, Inception v1,2,3, VGG-16,19, Xception, DenseNet121, EfficientNet B0	80,71,86,71, 82.80,82.75, 83.60, 79, 85.25, 86, 86.55, 73.60
(Cui and Liu, 2019a)	Histogram data winsorisation	CNN	99
(Costafreda et al., 2011)	DPARSF	CNN	92.06
(Korolev et al., 2017)	PANDA Skull-stripping	VoxCNN	79
(Wang et al., 2018)	Entropy-based sorting mechanism	ResNet VGG 16 Inception v4	80 92.3 96.25
(Ding et al., 2019)		CNN- Inception V3	82
(Zhang et al., 2011)	SMOTE technique	CNN	84.83
(Zhang et al., 2015)	ImageDataGenerator	CNN VGG-16 VGG-19	71.02 77.04 77.66
(Li and Liu, 2019a)	Skull stripping, Voxel intensity standardization,	CNN-VGG-16 (2D+C) VGG-16(3D) AlexNet(2D+C) AlexNet(3D)	92.3 89.8 89.2 88.6
(Sarraf and Tofghi., April, 2021)	Skull stripping, and spatial smoothing High-pass temporal filtering	CNN-LeNet	96.86
(Cui and Liu, 2019b)	ROI extraction	CNN Transfer Learning	88.10 92.86
(Cui et al., 2019)	Skull stripping	CNN	69.9
(Zaabi et al., 2020)	Data augmentation	DeepCNN, Inception-V4 ReNet	93 75 82
(Islam and Zhang, April, 2022)	Skull-stripped, Orientation adjusted	Deep Feed Forward Neural Network	99
(Yanga, f et al., 2011)	Statistical Parametric Mapping	CNN- AlexNet VGG-16 VGG-19 ResNet50 DenseNet50	76.53 77.82 79.37 81.42 80.38
(Ahmed et al., 2019)	Data imaging through grid method Brain voxel through Otsu threshold	CNN-Inception V3	82
(Spasov et al., 2018)	Large Deformation Diffeomorphic Metric Mapping (LDDMM) Algorithm	Graph-CNN	85.8
(Li et al., 2019)	Graph Neural Network Bilateral hippocampal region segmentation	CNN	i 90 ii 92

(continued on next page)

Table 2 (continued)

Reference Number	Pre-processing Techniques	Algorithms Utilized	Accuracy
Machine Learning Algorithms			
(Ieracitano et al., 2019a)	Anterior Commissure Posterior Commissure reorientation using MIPAV Software	CNN FSBi-LASTM	94.82
(Ieracitano et al., 2020)	N3 algorithm Skull Stripping HAMMER warping algorithm	CNN RNN CNN+RNN	88.99 85.01 91.33
(Sato et al., 2019)	Batch normalization	Deep Learning Classifiers	i 90 ii 95.8
(Chitradevi and Prabha, 2020)	N3 algorithm Skull stripping	LeNet VGGNet DenseBlock 1 DenseBlock 2 DenseBlock 3 DenseBlock 4	82.17 83.86 81.93 87.95 88.67 90.12
(Abdullahi et al., 2011)	Skull stripping N3 algorithm	LeNet VGGNet DenseNet	83.8 84.7 86.6
(Fisher et al., 2019)	Histogram Equalization	CNN-InceptionV3	85.7

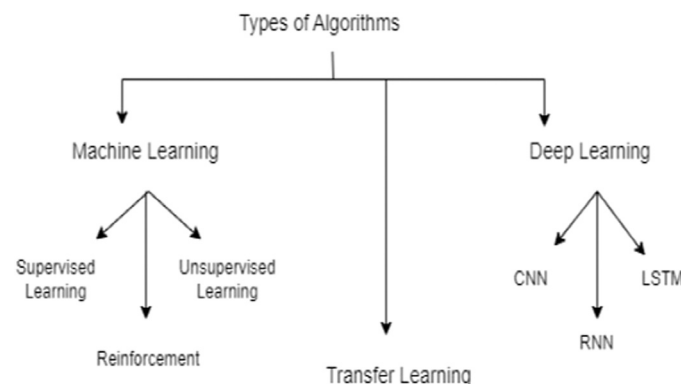


Fig. 3. An illustration for the different types of algorithms used for diagnosing Alzheimer's Disease.

process. Fig. 3 provides a concise overview of the assortment of AI algorithms utilized for Alzheimer's Disease diagnosis. It visually captures the algorithmic diversity within this diagnostic context.

4.1. Machine learning

A branch of AI called machine learning involves creating algorithms and statistical models that let computers learn from experience and become better at completing tasks. These models and algorithms are built to learn from data and predict or decide without being given specific instructions. Reinforcement learning, unsupervised learning, and supervised learning stand as the three primary forms of machine learning. In comparison to unsupervised learning, which includes training a model on unlabelled data, supervised learning involves developing a model on labelled data. Through trial and error, a model is trained through reinforcement learning. Natural language processing, image and voice recognition, and other fields all make use of machine learning.

The research is based on the image classification for AD. Naami et al.'s (Al-Naami et al., 2013) classification of CN from AD also used ANN, to achieve reliable efficiency and take advantage of the inherent correlation between features. Joshi et al (Joshi et al., 2010). examined different classification algorithms, including ANN, RBFNN, RF, Best-First decision tree (BF tree), DT, bagging and MLP for the

categorization of AD and Parkinson's disease. In real world situation, it's possible that not all the neuroimaging data needed to train on hand. The batch training method won't work in these circumstances. In order to achieve, Mahanand et al (Mahanand et al., 2012). classified AD using a self-adaptive resource allocation network (SRAN) algorithm.

When working the high dimensionality data, Mahmood et al (Mahmood and Ghimire, 2013). applied PCA method for dimensionality reduction and classified using artificial neural network. Cui et al (Cui et al., 2018). cascaded a Multilayer Perceptron and a Bidirectional Gated Recurrent Unit (BGRU) longitudinal data of MRI images. The LSTM memory network was used by Fritsch et al (Fritsch et al., 2019). to detect AD using information from sequential auditory recordings. Using DTI images, Kar et al (Kar and Majumder, 2019). used a fuzzy method with Artificial Neural Network to differentiate AD and Normal Control subjects. For the categorization of NC and AD, Long et al (Long and Wyatt, 2010). use an unsupervised method. The Fig. 4 represents classification framework for the machine learning algorithms.

In Fig. 4, illustrates the classification framework for the Machine Learning algorithm, the data of images are given as input and data split is done with 80% of training data and 20% of testing data. The features are extracted from training dataset for training the network. The trained classification model employs the testing set to anticipate labels, enabling the early AD detection.

Dominguez et al (Hernández-Domínguez et al., 2018). examined the effectiveness of RF and SVM. Shen Lu (Lu et al., 2017) uses the RF-SVM and knn-SVM methods. Additionally, RF showed outstanding performance on features obtained through Fusion of multiple modalities, including MRI, PET, genetic information, and CSF data (Glenn Clark et al., 2016; Gray et al., 2013; Lebedev et al., 2014). Hor et al (Hor and Moradi, 2016). introduced MRI and PET scans with tree-based feature transformations and applied RF for classification.

Escudero et al (Escudero et al., 2013). employed two classification tasks—AD-NC and cMCI-nMCI—using a machine learning technique for customised and cost-effective AD detection based on local weighted learning to minimise their number or expense for their diagnosis. In order to determine which classifier would be the most effective for diagnosing AD, Javier Escudero (Escudero et al., 2011) tested LR, SVM, RBF, and C4.5 classifiers. A. Illan et al (Illan et al., 2010). applied the Principal Component Analysis (PCA) method and used two kernels with the SVM: linear and Radial Basis Function (RBF).

4.2. Deep learning

A computer model that uses deep learning, learns to carry out classification tasks from images, text, or sound. Training the models involves utilizing an extensive dataset with labelled instances and multi layered neural network. Deep learning techniques are frequently referred to as "deep neural networks" since they frequently make use of neural network structures. In DL models, Convolutional Neural Networks are among the most popular. (ConvNet or CNN). Due to its integration of feature learning with input data and utilization of 2D convolutional layers, a CNN is especially adept at handling two-dimensional data, such as images. A machine learning method begins with manually extracting relevant features from images. Relevant features are automatically retrieved from images using DL approach. Deep learning also accomplishes "end-to-end learning," where a network is given unprocessed data and a task to complete, such as classification, and it automatically learns how to do this. Ortiz et al (Andres Ortiz et al., 2016). obtained 3D patches by employing an Automated Anatomical Labelling (AAL) atlas and subsequently conducted training for a DBN. Extraction of features utilising DBN (FEDBN-SVM) architecture yields the highest classification accuracy.

Deep CNN and Joint Linear LR (JLLR) of sparse regression are the two distinct models integrated by Suk et al (Suk et al., 2017). Suk et al (Suk and Shen, 2016). made a clinical diagnosis of AD using a deep CNN known as the Deep Ensemble Sparse Regression network (DeepESRNet)

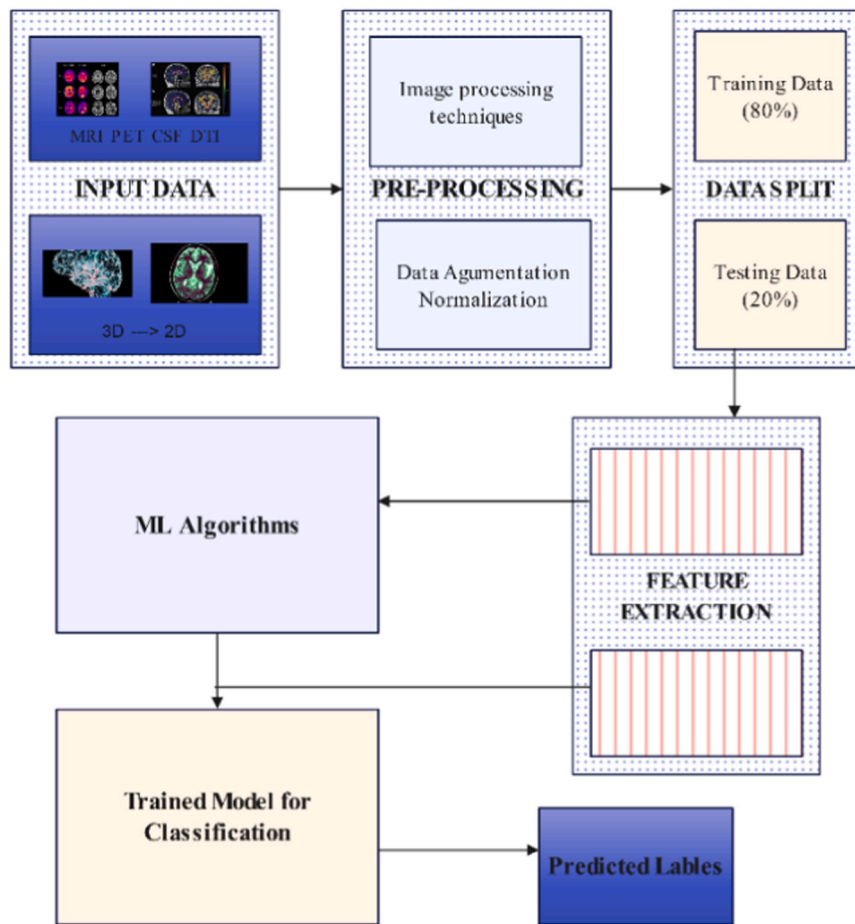


Fig. 4. Classification Framework for Machine Learning Algorithm.

and sparse regression models. By combining and learning from multi-modal neuroimaging data, the MultiModal Stacked Deep Polynomial Networks (MM-SDPN) algorithm was used by Shi et al (Shi et al., 2018). Algorithms based on the MM-SDPN are said to be better than the SAE. Using 3D sMRI (T1), Basaia et al (Basaia et al., 2018). developed a DL algorithm for the prediction of MCI patients who will be converted as AD in 36 months. It has been demonstrated that the CNN-based architecture is capable of differentiating CN from AD, MCI patients.

Deep CNN was utilised by Spasov et al (Spasov et al., 2019). extracted features from sMRI for the classification of AD, CNN efficiently selects the parameters. SAE was used by Suk et al (Suk and Shen, 2013). to demonstrate the characteristics of non-linear correlations can increase the accuracy of diagnosing AD. Patch-based characteristics from MRI and PET were combined by Suk et al (Suk et al., 2014). to classify AD using a deep Boltzmann machine. (DBM). When SAE and CNN were combined, Payan et al (Payan and Montana, 2015). discovered that 3D-CNN performed better at classifying AD and MCI from NC. Suk et al (Suk et al., 2015). used an SAE-based classifier and a DL-based latent feature representation. The most accurate results were obtained using a Multi-kernel SVM with Low-Level features (LLF) and SAElearned features. (SAEF).

SAE-based DL architecture was used by Liu et al (Suk and Shen, 2013). to detect AD in four stages. Suk et al (Suk et al., 2016). used the biomarker of the MCI diagnosis and combines deep learning and state space models, and functional dynamics with time of rs-fMRI. DL multi-scale DNN (MDNN) was developed by Lu et al (Lu et al., 2018). utilized singular modality data, specifically FDG-PET images, and showcased the improved discriminative capacity of the deep learning architecture for AD diagnosis. When using various validation parameters, grouping of

many classifiers improves classification performance and is more reliable and stable. Wang et al (Wang et al., 2019). formulated an ensemble comprised of 3D densely connected CNNs, recognized by the name 3D-DenseNets.

When using sMRI images to diagnose AD, it prevents over-fitting and improves performance. The study to combine fMRI data with deep learning is Sarraf et al (Sarraf et al., 2017). Helaly et al (Helaly et al., 2022). used CNN architecture and applied transfer learning to compare the results of AD diagnosis. Lee et al (Lee et al., 2019a). developed an integrative framework using a DL approach, multimodal Recurrent Neural Network (RNN), which combines Cerebro-Spinal Fluid (CSF) and cognitive performance biomarkers, with cross-sectional neuroimaging biomarkers. Albright et al (Albright, 2019). and Fan Li (Li and Liu, 2019b) used RNN architecture. Lee et al (Lee et al., 2019a). proposed a novel method, that systematically integrates voxel-based, region-based, and patch-based approaches into framework with deep feed forward neural network and SVM for classification. The Fig. 5 portrays a classification framework designed for the application of a deep learning algorithm. The input involves data which undergoes preprocessing and feature extraction using deep learning algorithms, all directed towards the classification intended for Alzheimer's Disease diagnosis.

4.3. Transfer learning

The process of transferring knowledge from one model to another is known as transfer learning in deep learning (and machine learning). Transfer learning is the process of applying a previously learnt model to a new model. It is now highly utilised in deep learning due to the ability to train deep neural networks using a small amount of data. Several

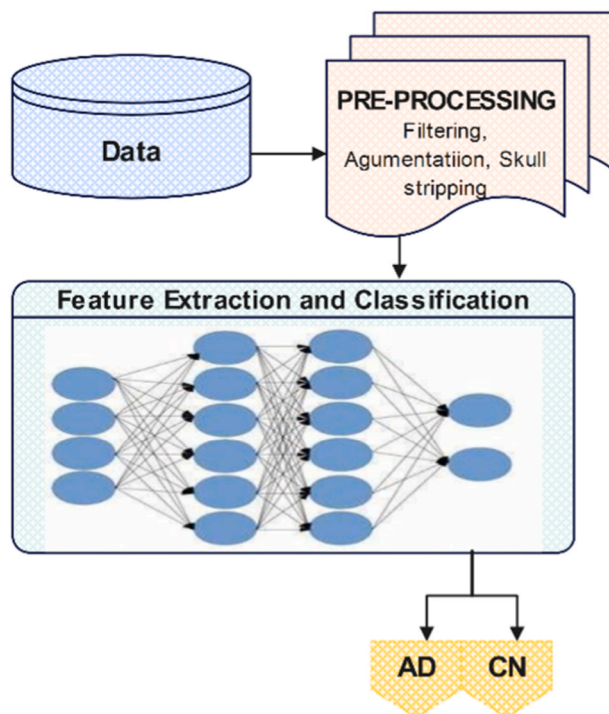


Fig. 5. Classification Framework Utilizing deep learning Algorithm for AD Diagnosis.

different methods can be used to implement transfer learning in the deep and machine learning domains. The three basic methods for applying transfer learning to deep learning models are as follows. The direct use of trained models, extracting the features from the trained models, and fine-tuning the last layer of pre-trained models. Ramzan et al. (2020). applied transfer learning, employing an extended ResNet18 architecture, both with and without fine-tuning, to evaluate the accuracy of rs-fMRI data in multi class classification for AD analysis.

Mehmood et al. (2021). applied layer-wise transfer learning using VGG19 and integrated brain image tissue segmentation to facilitate early-stage Alzheimer's Disease diagnosis. Hazarika et al. (null). applied CNN such as ResNet, DenseNet, VGG and AlexNet. Among which DenseNet with depth-wise convolution approach obtains the highest performance. Janghel and Rathore (2021). applied 3D to 2D conversion method and transfer learning (VGG-16 architecture) for feature extraction. The classification methods used for AD detection are SVM, Linear Discriminate, K means clustering, and DT.

The performance of the model is compromised by the transfer of knowledge from diverse source domains, including those that are unrelated. Additionally, the various samples' class labels could be incorrect. To address these issues, Liu et al. (2020a). applied robust Multi-Label Transfer Learning (rMLTFL) method to convert the original label into multi-bit label coding vectors. Choi and Lee (2020) used the VGG, GoogleNet and AlexNet of CNN architecture with SoftMax layer. Using the subspace alignment approach, Li et al. (2018). utilized ADNI samples to transfer the knowledge gained from an actual domain (CN vs. AD) to facilitate the learning of the predicting domain, Cheng et al (Cheng et al., 2015). used the multimodal manifold regularised Transfer Learning (M2TL). Jain et al. (2019). applied the transfer learning VGG16 architecture and fine-tuning method.

The TrAdaBoost method was applied by Zhou et al. (2018). on AD diagnosis. Chen et al (Chen et al.,). used the Iterative Sparse Deep Learning (ISDL) model for feature extraction and crucial cortical region identification and ResNet10 network was used to diagnose AD and MCI. Nigri et al. (2020b). applied AlexNet and VGG16 for the 2D sagittal and 3D images. Bae et al. (2021). used transfer learning to the target task of

pMCI vs. sMCI from the trained ResNet29 on the AD vs. NC task classification was used by Bae et al. (2021). Afzal et al.'s (Afzal et al., 2019) used fine-tuning and transfer learning of a pre-trained AlexNet (Raza et al., 2019; Fang et al., 2020). Ieracitano et al. (2019a). took a step further and developed a multi domain TL model in their subsequent work. (MDTL) (Dong et al., 2019). compares the transfer learning (AlexNet, ResNet and GoogleNet) (Ebrahimi-Ghahnavieh et al., 2019). used the transfer learning in CNN for feature representation of slices and LSTM model (Khan et al., 2019). fine turning by different layers of network with transfer learning of VGG19 architecture.

The depicted transfer learning model in Fig. 6 exemplifies a robust approach to leveraging pre-trained neural networks for improved learning in new tasks. By reusing the knowledge gained from a source domain, the model efficiently adapts its understanding to a target domain, thereby enhancing performance and reducing the need for extensive training data. Subsequently, these adapted features are employed in a classification task, highlighting the model's ability to enable effective problem-solving. From the survey conducted, a comparative analysis of percentage of machine learning, deep learning and transfer learning methods applied for dementia detection is represented in Fig. 7.

5. Conclusion and future work

In conclusion, our study encompasses a comprehensive comparative analysis of research papers spanning from 2011 to the present, focused on the early Alzheimer's Disease detection using three distinct AI methodologies: Machine Learning, Deep Learning, and Transfer Learning. Our approach was multifaceted, involving three main stages. Initially, we meticulously curated a collection of 50 papers, each highlighting the datasets employed in AD diagnosis. This compilation showcased variations in input types, subject quantities, and classes utilized. Subsequently, our attention shifted towards refining the models for AD detection by concentrating on pre-processing techniques and algorithms. Through the thorough examination of 60 papers, we succinctly outlined the methodologies employed to achieve enhanced accuracy. These methodologies revolved around the pillars of machine learning, deep learning, and transfer learning, collectively forming the bedrock of early AD diagnosis.

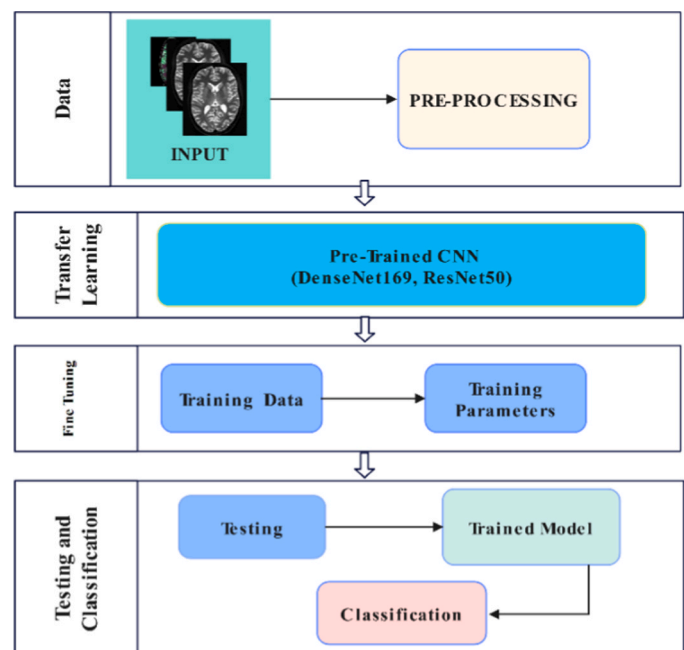


Fig. 6. Transfer Learning Model.

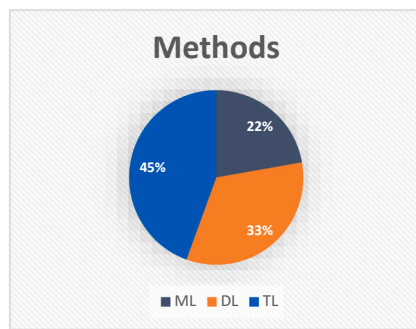


Fig. 7. A comparative diagram for the Machine Learning, Deep Learning and Transfer Learning methods used for Alzheimer's Dementia Detection.

The extensive utilization of tables and figures within our work provides invaluable guidance to fellow researchers, enabling them to adeptly select datasets and architectures best suited for their predictive AD research endeavours. From our survey, a notable trend emerges: the integration of neuro images, accompanied by skilful feature extraction and the application of appropriate AI techniques, stands as a dominant approach in the timely identification of AD. As we peer into the future, our research postulates that the integration of novel AI models, particularly those incorporating federated learning, could offer fresh perspectives on early AD diagnosis. Furthermore, while our survey predominantly concentrated on neuro images as a single modality data source, we anticipate that forthcoming investigations will broaden their horizons to encompass diverse modalities such as emotions, speech, and text datasets. This expansion could herald a transformative era in the early diagnosis of dementia-related diseases. In essence, our paper contributes to the field by synthesizing a wealth of contemporary research, shedding light on the effectiveness of various AI methodologies in AD diagnosis. The methodical analysis of datasets, techniques, and trends presented herein empowers researchers to navigate the intricate landscape of AD detection with heightened precision and insight. Our findings underscore the pivotal role that AI, in its multifaceted forms, plays in advancing our ability to detect and understand AD at its nascent stages.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements and funding

This work was supported the Korea Environmental Industry & Technology Institute (KEITI), with a grant funded by the Korea government, Ministry of Environment (The development of IoT-based technology for collecting and managing big data on environmental hazards and health effects), under Grant RE202101551 and partially supported by the Institute of Information and Communications Technology Planning and Evaluation (IITP) funded by the Korea Government, Ministry of Science and ICT (MSIT) (Building a Digital Open Lab as open innovation platform) under Grant 2021-0-00546.

References

Abdullah1, Noramalina, Ngah2, Umi Kalthum, Aziz, Shalihatan Azlin, 2011. Image classification of brain MRI using support vector machine. *IEEE Int. Conf. Imaging Syst. Tech.*

Abrol, Anees, Fu, Zening, Du, Yuhui, Calhoun, Vince D., 2019. Multimodal data fusion of deep learning and dynamic functional connectivity features to predict Alzheimer's disease progression. *International Conference of EMBC. IEEE* 2019, pp. 4409–4413.

Acharya, Heta, Mehta, Rutvik, Kumar Singh, Dheeraj, 2021. Alzheimer's disease classification using transfer learning. *ICCMC volume* 1528.

Adeola Ajagbe1, Sunday, Amuda, Kamoruadeen A., Oladipupo, Matthew A., Kikelomo, Oluwaseyi F., Okesola, 2019. Multi-classification of alzheimer disease on magnetic resonance images (MRI) using deep convolutional neural network (DCNN) approaches. *Int. J. Adv. Comput. Res. Vol* 11 (53).

Afzal, S., Maqsood, M., Nazir, F., Khan, U., Aadil, F., Awan, K.M., Mehmood, I., Song, O.-Y., 2019. A data augmentation-based framework to handle class imbalance problem for Alzheimer's stage detection. *IEEE Access* 7, 115528–115539.

Ahmed, S., Choi, K.Y., Lee, J.J., KIM, B.C., Kwon, G.-R., Lee, K.H., Jung, H.Y., 2019. Ensembles of patch-based classifiers for diagnosis of Alzheimer diseases. *IEEE Access* 7, 73373–73383.

Albright, J., 2019. Forecasting the progression of Alzheimer's disease using neural networks and a novel preprocessing algorithm. *Alzheimers Dement* 5 (1), 483–491.

Al-Naami, B., Gharaibeh, N., AlRazzaq Kheshman, A., 2013. Automated detection of Alzheimer's disease using region growing technique and artificial neural network. *World Acad. Sci. Eng. Technol. Int. J. Biomed. Biol. Eng.* 7 (2013), 5.

AlSaeed, Duaa, Omar, Samar Fouad, 2022. Brain MRI analysis for Alzheimer's disease diagnosis using CNN-based feature extraction and machine learning. *Sensors* 22 (8), 2911.

An, N., Ding, H., Yang, J., Au, R., Ang, T.F., 2020. Deep ensemble learning for Alzheimer's disease classification. *J. Biomed. Inf.* 105 (February), 103411.

Andres Ortiz, Munilla, Jorge, Gorriz, Juan M., Ramirez, Javier, 2016. Ensembles of deep learning architectures for the early diagnosis of the Alzheimer's disease. *Int. J. Neural Syst.* 26 (2016), 1650025, 7.

Bae, J., Stocks, J., Heywood, A., Jung, Y., Jenkins, L., Hill, V., Katsaggelos, A., Popuri, K., Rosen, H., Beg, M.F., Wang, L., 2021. Transfer learning for predicting conversion from mild cognitive impairment to dementia of Alzheimer's type based on a three-dimensional convolutional neural network. *Neurobiol. Aging* 99, 53–64.

Basaia, S., Agosta, F., Wagner, L., Canu, E., Magnani, G., Santangelo, R., Filippi, M., 2019a. Automated classification of Alzheimer's disease and mild cognitive impairment using a single MRI and deep neural networks. *NeuroImage* 21 (October 2018), 101645.

Basaia, S., Agosta, F., Wagner, L., Canu, E., Magnani, G., Santangelo, R., Filippi, M., 2019b. Automated classification of Alzheimer's disease and mild cognitive impairment using a single MRI and deep neural networks. *NeuroImage* 21 (October 2018), 101645.

Basaia, Silvia, Agosta, Federica, Wagner, Luca, Canu, Elisa, Magnani, Giuseppe, Santangelo, Roberto, Filippi, Massimo, Neuroimaging Initiative, Alzheimer's Disease, et al., 2018. Automated classification of Alzheimer's disease and mild cognitive impairment using a single MRI and deep neural networks. *NeuroImage: Clin.* (2018), 101645.

Bi, X., Wang, H., 2019. Early Alzheimer's disease diagnosis based on EEG spectral images using deep learning. *Neural Netw.* 114, 119–135.

Y. Chen, Y. Xia, Iterative sparse and deep learning for accurate diagnosis of Alzheimer's disease, *Pattern Recognition* 116. doi:10.1016/j.patrec.2021.107944.

Cheng, Bo, Liu, Mingxia, Suk, Heung-Il, Shen, Dinggang, Zhang, Daoqiang, Alzheimer's Disease Neuroimaging Initiative, 2015. Multimodal manifold-regularized transfer learning for MCI conversion prediction. *Brain Imag. Behav.* 9 (2015), 913–926, 4.

Chitradevi, D., Prabha, S., 2020. Analysis of brain sub regions using optimization techniques and deep learning method in alzheimer disease. *Appl. Soft Comput.* 86, 105857.

Choi, J.Y., Lee, B., 2020. Combining of multiple deep networks via ensemble generalization loss, based on MRI images, for Alzheimer's disease classification. *IEEE Signal Process. Lett.* 27, 206–210.

Costafreda, S.G., Dinov, I.D., Tu, Z., Shi, Y., Liu, C.-Y., Kloszewska, I., Mecocci, P., Soininen, H., Tsolaki, M., Vellas, B., Wahlund, L.-O., Spenger, C., Toga, A.W., Lovestone, S., Simmons, A., 2011. Automated hippocampal shape analysis predicts the onset of dementia in mild cognitive impairment. *Neuroimage* 56 (1), 212–219.

Cui, R., Liu, M., 2019a. RNN-based longitudinal analysis for diagnosis of Alzheimer's disease. *Comput. Med Imaging Graph* 73, 1–10.

Cui, R., Liu, M., 2019b. Hippocampus analysis by combination of 3-D DenseNet and shapes for Alzheimer's disease diagnosis. *IEEE J. Biomed. Health Inf.* 23 (5), 2099–2107.

Cui, Ruoxuan, Liu, Manhua, Li, Gang, 2018. Longitudinal analysis for Alzheimer's disease diagnosis using RNN. In *Proceedings of the IEEE 15th International Symposium on Biomedical Imaging (ISBI'18)*. IEEE, pp. 1398–1401.

Cui, Z., Gao, Z., Leng, J., Zhang, T., Quan, P., Zhao, W., 2019. Alzheimer's disease diagnosis using enhanced inception network based on brain magnetic resonance image. In: *IEEE international conference on bioinformatics and biomedicine (BIBM)*, 2019. IEEE, pp. 2324–2330.

Ding, Y., Sohn, J.H., Kawczynski, M.G., Trivedi, H., Harnish, R., Jenkins, N.W., Lituev, D., Copeland, T.P., Aboian, M.S., Aparici, C.Mari, Behr, S.C., Flavell, R.R., Huang, S.-Y., Zalocusky, K.A., Nardo, L., Seo, Y., Hawkins, R.A., Pampaloni, M., Hernandez, Hadley, D., Franc, B.L., 2019. A deep learning model to predict a diagnosis of Alzheimer disease by using 18 F-FDG PET of the brain. *Radiology* 290 (2), 456–464.

Dong, Q., Zhang, J., Li, Q., Thompson, P.M., Caselli, R.J., Ye, J., Wang, Y., 2019. Multi-task dictionary learning based on convolutional neural networks for longitudinal clinical score predictions in Alzheimer's disease. In: *Communications in computer and information science*, 1072. Springer, Singapore, pp. 21–35.

Duc, N.T., Ryu, S., Qureshi, M.N.I., Choi, M., Lee, K.H., Lee, B., 2020. 3D-deep learning based automatic diagnosis of Alzheimer's disease with joint MMSE prediction using resting-state fMRI. *Neuroinformatics* 18 (1), 71–86.

Ebrahimi-Ghahnavieh, A., Luo, S., Chiong, R., 2019. Transfer learning for Alzheimer's disease detection on MRI images. *IEEE Int. Conf. Ind. 4. O. Artif. Intell., Commun. Technol. (IAICT)* 2019, 133–138.

- Escudero, Javier, Ifeachor, Emmanuel, Zajicek, John P., Green, Colin, Shearer, James, Pearson, Stephen, 2013. Machine learning-based method for personalized and cost-effective detection of Alzheimer's disease (JANUARY). *IEEE Trans. Biomed. Eng.* VOL. 60 (JANUARY).
- Javier Escudero, John P. Zajicek, Emmanuel Ifeachor. Machine Learning Classification of MRI Features of Alzheimer's Disease and Mild Cognitive Impairment Subjects to Reduce the Sample Size in Clinical Trials. *International Conference of the IEEE EMBS*, September 2011.
- Fang, X., Liu, Z., Xu, M., 2020. Ensemble of deep convolutional neural networks based multi-modality images for Alzheimer's disease diagnosis. *IET Image Process* 14 (2), 318–326.
- Fisher, C.K., Smith, A.M., Walsh, J.R., 2019. Machine learning for comprehensive forecasting of Alzheimer's disease progression. *Sci. Rep.* 9 (1), 13622.
- Julian Fritsch, Sebastian Wankerl, and Elmar Nöth. 2019. Automatic diagnosis of Alzheimer's disease using neural network language models. In *Proceedings of the IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP'19)*. IEEE, 5841–5845.
- Glenn Clark, David, McLaughlin, Paula M., Woo, Ellen, Hwang, Kristy, Hertz, Sona, Ramirez, Leslie, Eastman, Jennifer, Dukes, Reshil-Marie, Kapur, Puneet, DeRamus, Thomas P., et al., 2016. Novel verbal fluency scores and structural brain imaging for prediction of cognitive outcome in mild cognitive impairment. *Alzheimer's Dementia. Diagn. Assess. Dis. Monit.* 2 (2016), 113–122.
- Gray, Katherine R., Aljabar, Paul, Heckemann, Rolf A., Hammers, Alexander, Rueckert, Daniel, Neuroimaging Initiative, Alzheimer's Disease, et al., 2013. Random forest-based similarity measures for multi-modal classification of Alzheimer's disease. *NeuroImage* 65 (2013), 167–175.
- Gunawardena, K.A.N.N.P., Rajapakse, R.N., Kodikara, N.D., 2017. Applying convolutional neural networks for pre-detection of Alzheimer's disease from structural MRI data. *International Conference on M2VIP*. IEEE.
- R.A. Hazarika D. Kandar A.K. Maji, An experimental analysis of different deep learning based models for Alzheimer's disease classification using brain magnetic resonance images, *J King Saud Univ Comput Information Sci* doi:10.1016/j.jksuci.2021.09.003.
- Hazarika, Ruhul Amin, Maji, Arnab Kumar, Kandar, Debdatta, Jasinska, Elzbieta, Krejci, Petr, Leonowicz, Zbigniew, Jasinski, Michal, 2023. An approach for classification of Alzheimer's disease using deep neural network and brain magnetic resonance imaging (MRI). *Electronics* 12 (3), 676.
- Helaly, Hadeer A., Badawy, Mahmoud, Haikal, Amira Y., 2022. Deep learning approach for early detection of Alzheimer's disease. *Springer* 14 (5), 1711–1727.
- Hernández-Domínguez, Laura, Ratté, Sylvie, Sierra-Martínez, Gerardo, Roche-Bergua, Andrés, 2018. Computer based evaluation of Alzheimer's disease and mild cognitive impairment patients during a picture description task. *Alzheimer's Dementia. Diagn. Assess. Dis. Monit.* 10 (2018), 260–268.
- Hon, Marcia, Khan, Naimul Mefraz, 2017. Towards Alzheimer's disease classification through transfer learning. *IEEE Int. Conf. BIBM*.
- Hor, Soheil, Moradi, Mehdi, 2016. Learning in data-limited multimodal scenarios: scendent decision forests and tree-based features. *Med. Image Anal.* 34 (2016), 30–41.
- Ieracitano, C., Mammone, N., Bramanti, A., Hussain, A., Morabito, F.C., 2019a. A convolutional neural network approach for classification of dementia stages based on 2Dspectral representation of EEG recordings. *Neurocomputing* 323, 96–107.
- Ieracitano, C., Mammone, N., Bramanti, A., Marino, S., Hussain, A., Morabito, F.C., 2019b. A time-frequency based machine learning system for brain states classification via EEG signal processing. *Int. Jt. Conf. Neural Netw. (IJCNN)* 2019, 1–8.
- Ieracitano, C., Mammone, N., Hussain, A., Morabito, F.C., 2020. A novel multi-modal machine learning based approach for automatic classification of EEG recordings in dementia. *Neural Netw.* 123, 176–190.
- A. Illan, J.M. Gorris, J. Ram irez, R. Chaves, F. Segovia, M. Lopez, D. Salas-Gonzalez, P. Padilla C.G. Puntonet Machine learning for very early Alzheimer's Disease diagnosis; a 18F-FDG and PiB PET comparison. 2010 IEEE.
- Islam, Jyoti, Zhang, Yanqing, 2022. Brain MRI analysis for Alzheimer's disease diagnosis using an ensemble system of deep convolutional neural networks. *Sensors* 22 (8), 2911.
- Jain, R., Jain, N., Aggarwal, A., Hemanth, D.J., 2019. Convolutional neural network based Alzheimer's disease classification from magnetic resonance brain images. *Cogn. Syst. Res* 57, 147–159.
- Janghel, R.R., Rathore, Y.K., 2021. Deep convolution neural network based system for early diagnosis of Alzheimer's disease. *IRBM* 42 (4), 258–267.
- Joshi, Sandhya, Shenoy, Deepa, Rrashi, P.L., Venugopal, K.R., Patnaik, L.M., 2010. Classification of Alzheimer's disease and parkinson's disease by using machine learning and neural network methods. *Proc. 2nd Int. Conf. Mach. Learn. Comput. IEEE* 218–222.
- Kar, Subrata, Majumder, D.Dutta, 2019. A novel approach of diffusion tensor visualization-based neuro fuzzy classification system for early detection of Alzheimer's disease. *J. Alzheimer's Dis. Rep.* 3 (2019), 1–18, 1.
- Khan, N.M., Abraham, N., Hon, M., 2019. Transfer learning with intelligent training data selection for prediction of Alzheimer's disease. *IEEE Access* 7, 72726–72735.
- H.W. Kim H.E. Lee S. Lee K.T. Oh M. Yun S.K. Yoo Slice-selective learning for Alzheimer's disease classification using a generative adversarial network: a feasibility study of external validation *Eur J Nucl Med Mol Imaging* doi:10.1007/s00259-019-04676.
- Korolev, Sergey, Mikhail Belyaev, Amir Saffullin, Dodonova, Yulia, 2017. Residual and plain convolutional neural networks for 3d Brain MRI classification. *IEEE 14th Int. Symp. Biomed. Imaging* 16965512.
- Lebedev, A.V., Westman, Eric, Van Westen, G.J.P., Kramberger, M.G., Lundervold, Arvid, Aarsland, Dag, Soininen, H., Kłoszewska, I., Mecocci, P., Tsolaki, M., et al., 2014. Random forest ensembles for detection and prediction of Alzheimer's disease with a good between-cohort robustness. *NeuroImage: Clin.* 6 (2014), 115–125.
- Lee, G., Nho, K., Kang, B., Sohn, K.-A., Kim, D., 2019a. Predicting Alzheimer's disease progression using multi-modal deep learning approach. *Sci. Rep.* 9 (1), 1952.
- Li, F., Liu, M., 2019a. A hybrid convolutional and recurrent neural network for hippocampus analysis in Alzheimer's disease. *J. Neurosci. Methods* 323, 108–118.
- Li, F., Liu, M., 2019b. A hybrid convolutional and recurrent neural network for hippocampus analysis in Alzheimer's disease. *J. Neurosci. Methods* 323, 108–118.
- Li, H., Habes, M., Wolk, D.A., Fan, Y., 2019. A deep learning model for early prediction of Alzheimer's disease dementia based on hippocampal magnetic resonance imaging data. *Alzheimers Dement* 15 (8), 1059–1070.
- Li, Wei, Zhao, Yifei, Chen, Xi, Xiao, Yang, Qin, Yuan, 2018. Detecting Alzheimer's disease on small dataset: a knowledge transfer perspective. *IEEE J. Biomed. Health Info* 23 (2018), 1234–1242, 3.
- Liu, C.-F., Padhy, S., Ramachandran, S., Wang, V.X., Efimov, A., Bernal, A., Shi, L., Vaillant, M., Ratnanather, J.T., Faria, A.V., Caffo, B., Albert, M., Miller, M.I., 2019. Using deep Siamese neural networks for detection of brain asymmetries associated with Alzheimer's disease and mild cognitive impairment. *Magn. Reson Imaging* 190–199.
- Liu, M., Zhang, J., Adeli, E., Shen, D., 2019. Joint classification and regression via deep multitask multi-channel learning for Alzheimer's disease diagnosis. *IEEE Trans. Biomed. Eng.* 66 (5), 1195–1206.
- Liu, M., Lian, C., Shen, D., 2020a. Anatomical-landmark-based deep learning for Alzheimer's disease diagnosis with structural magnetic resonance imaging. *Intell. Syst. Ref. Libr.* 171, 127–147.
- Liu, M., Li, F., Yan, H., Wang, K., Ma, Y., Shen, L., Xu, M., 2020b. A multi-model deep convolutional neural network for automatic hippocampus segmentation and classification in Alzheimer's disease. *NeuroImage* 208 (August 2018), 116459.
- Long, Xiaojing, Wyatt, Chris, 2010. An automatic unsupervised classification of MR images in Alzheimer's disease. In *Proceedings of the IEEE Computer Society Conference on Computer Vision and Pattern Recognition. IEEE*, pp. 2910–2917.
- Lu, Donghuan, Popuri, Kartek, Weiguang Ding, Gavin, Balachandrar, Rakesh, Faisal Beg, Mirza, Alzheimer's Disease Neuroimaging Initiative, et al., 2018. Multiscale deep neural network-based analysis of FDG-PET images for the early diagnosis of Alzheimer's disease. *Med. Image Anal.* 46 (2018), 26–34.
- Lu, Shen, Xia, Yong, Cai, Weidong, Fulham, Michael, Feng, David Dagan, Neuroimaging Initiative, Alzheimer's Disease, et al., 2017. Early identification of mild cognitive impairment using incomplete random forest-robust support vector machine and FDG-PET imaging. *Comput. Med. Imag. Graph.* 60 (2017), 35–41.
- Mahanand, Belathur Suresh, Suresh, Sundaram, Sundararajan, Narasimhan, Kumar, M. Aswatha, 2012. Identification of brain regions responsible for Alzheimer's disease using a Self-adaptive resource allocation network. *Neural Netw.* 32 (2012), 313–322.
- Mahmood, Rigel, Ghimire, Bishad, 2013. Automatic detection and classification of Alzheimer's disease from MRI scans using principal component analysis and artificial neural networks. In *Proceedings of the 20th International Conference on Systems, Signals and Image Processing (IWSSIP'13)*. IEEE, pp. 133–137.
- Maqsood 1, Muazzam, Nazir 2, Faria, Khan 1, Umair, Aadil 1, Farhan, Jamal 3, Habibullah, Mehmood 4, Irfan, Song, Oh-young, 2019. Transfer learning assisted classification and detection of Alzheimer's disease Stages Using 3D MRI scans. *Sensors* 19 (11), 2645.
- Mehmood, A., Yang, S., Feng, Z., Wang, M., Ahmad, A.S., Khan, R., Maqsood, M., Yaqub, M., 2021. A transfer learning approach for early diagnosis of Alzheimer's disease on MRI images. *Neuroscience* 460, 43–52.
- Murugan, Suriya, Venkatesan, Chandran, Sumithra, M.G., (senior member, iee), Gao, Xiao-Zhi, Elakkiya, B., Akila, M., Manoharan, S., 2021. DEMNET: a deep learning model for early diagnosis of Alzheimer diseases and dementia from MR images. *IEEE Access* PP.
- Nigri, E., Ziviani, N., Cappabianco, F., Antunes, A., Veloso, A., 2020b. Explainable deep CNNs for MRI-based diagnosis of Alzheimer's disease. *Int. Jt. Conf. Neural Netw. (IJCNN)* 2020, 1–8.
- Nigri, Eduardo, Ziviani, Nivio, Cappabianco, Fabio, Antunes, Augusto, Veloso, Adriano, 2020a. Explainable deep CNNs for MRI-based diagnosis of Alzheimer's disease. *Int. Jt. Conf. Neural Netw. (IJCNN)* 20039093.
- Payan, Adrien, Montana, Giovanni, 2015. Predicting Alzheimer's disease: a neuroimaging study with 3D convolutional neural networks. *Arxiv Prepr. Arxiv* (2015), 1502.02506.
- Ramzan, F., Khan, M.U.G., Rehmat, A., Iqbal, S., Saba, T., Rehman, A., Mehmood, Z., 2020. A deep learning approach for automated diagnosis and multi-class classification of Alzheimer's disease stages using resting-state fMRI and residual neural networks. *J. Med Syst.* 44 (2), 37.
- Raza, M., Awais, M., Ellahi, W., Aslam, N., Nguyen, H., Le-Minh, H., 2019. Diagnosis and monitoring of Alzheimer's patients using classical and deep learning techniques. *Expert Syst. Appl.* 136, 353–364.
- Sarraf, Saman, Tofghi, Ghassem, 2021. Classification of Alzheimer's Disease Using fMRI Data and Deep Learning Convolutional Neural Networks, 53. Springer, pp. 2649–2663.
- Sarraf, Saman, DeSouza, Danielle D., Anderson, John, Tofghi, Ghassem, et al., 2017. DeepAD: Alzheimer's disease classification via deep convolutional neural networks using MRI and fMRI. *BioRxiv* (2017), 070441.
- Sato, R., Iwamoto, Y., Cho, K., Kang, D.-Y., Chen, Y.-W., 2019. Comparison of CNN models with different plane images and their combinations for classification of Alzheimer's disease using PET images. Springer, Singapore, pp. 169–177.
- Shi, Jun, Zheng, Xiao, Li, Yan, Zhang, Qi, Ying, Shihui, 2018. Multimodal neuroimaging feature learning with multimodal stacked deep polynomial networks for diagnosis of Alzheimer's disease. *IEEE J. Biomed. Health Info* 22 (2018), 173–183, 1.

- Silva, I.R.R., Silva, G.S.L., de Souza, R.G., dos Santos, W.P., Fagundes RAdE, A., 2019. Model based on deep feature extraction for diagnosis of Alzheimer's disease. In: July international joint conference on neural networks (IJCNN), Vol. 2019. IEEE.
- SK, L.S.K., Khanna, A., Tanwar, S., Rodrigues, J.J., Roy, N.R., 2019. Alzheimer detection using Group Grey Wolf-optimization based features with convolutional classifier. *Comput. Electr. Eng.* 77, 230–243.
- Sørensen, L., Igel, C., Pai, A., Balas, I., Anker, C., Lillholm, M., Nielsen, M., 2017. Differential diagnosis of mild cognitive impairment and Alzheimer's disease using structural MRI cortical thickness, hippocampal shape, hippocampal texture, and volumetry. *NeuroImage* 13, 470–482.
- Spasov, Simeon, Passamonti, Luca, Duggento, Andrea, Lio, Pietro, Toschi, Nicola, Neuroimaging Initiative, Alzheimer's Disease, et al., 2019. A parameter-efficient deep learning approach to predict conversion from mild cognitive impairment to Alzheimer's disease. *NeuroImage* 189 (2019), 276–287.
- Simeon E. Spasov, Luca Passamonti, Andrea Duggento, Pietro Liò, and Nicola Toschi. A Multi-modal Convolutional Neural Network Framework for the Prediction of Alzheimer's Disease. *International Conference of the IEEE Engineering in Medicine and Biology Society July 2018, 2018:1271–1274.*
- Suk, Heung-II, Shen, Dinggang, 2013. Deep learning-based feature representation for AD/MCI classification. In *Proceedings of the International Conference on Medical Image Computing and Computer-Assisted Intervention*. Springer, pp. 583–590.
- Suk, Heung-II, Shen, Dinggang, 2016. Deep ensemble sparse regression network for Alzheimer's disease diagnosis. In *Proceedings of the International Workshop on Machine Learning in Medical Imaging*. Springer, pp. 113–121.
- Suk, Heung-II, Lee, Seong-Whan, Shen, Dinggang, Neuroimaging Initiative, Alzheimer's Disease, 2014. Hierarchical feature representation and multimodal fusion with deep learning for AD/MCI diagnosis. *NeuroImage* 101 (2014), 569–582.
- Suk, Heung-II, Lee, Seong-Whan, Shen, Dinggang, Neuroimaging Initiative, Alzheimer's Disease, 2015. Latent feature representation with stacked auto-encoder for AD/MCI diagnosis. *Brain Struct. Funct.* 220 (2015), 841–859, 2.
- Suk, Heung-II, Wee, Chong-Yaw, Lee, Seong-Whan, Shen, Dinggang, 2016. State-space model with deep learning for functional dynamics estimation in resting-state fMRI. *NeuroImage* 129 (2016), 292–307.
- Suk, Heung-II, Lee, Seong-Whan, Shen, Dinggang, Neuroimaging Initiative, Alzheimer's Disease, 2017. Deep ensemble learning of sparse regression models for brain disease diagnosis. *Med. Image Anal.* 37 (2017), 101–113.
- Tang, Z., Chuang, K.V., DeCarli, C., Jin, L.-W., Beckett, L., Keiser, M.J., Dugger, B.N., 2019. Interpretable classification of Alzheimer's disease pathologies with a convolutional neural network pipeline. *Nat. Commun.* 10 (1), 2173.
- Wang, Hongfei, Shen, Yanyan, Wang, Shuqiang, Xiao, Tengfei, Deng, Liming, Wang, Xiangyu, Zhao, Xinyan, 2019. Ensemble of 3D densely connected convolutional network for diagnosis of mild cognitive impairment and alzheimer's disease. *Neurocomputing* 333 (2019), 145–156.
- Wang, Yan, Yang, Yanwu, Guo, Xin, Ye, Chenfei, Gao, Na, Fang, Yuan, Ma, Heather T., 2018. A novel multimodal MRI analysis for Alzheimer's disease based on convolutional neural network. *Int. Conf. IEEE (EMBC)* 18198106.
- Xiao, Zhe, Ding, Yi, Lan, Tian, Zhang, Cong, Luo, Chuanji, Qin, Zhiguang, 2017. Brain MR image classification for Alzheimer's disease diagnosis based on multifeature fusion. *Comput. Math. Methods Med.*, 1952373.
- Ekin Yagis, Luca Citi1, Stefano Diciotti, Chiara Marzi, Selamawet Workalemahu Atnafu, Alba G. Seco De Herrera. 3D Convolutional Neural Networks for Diagnosis of Alzheimer's Disease via structural MRI. *IEEE 33rd International Symposium on CBMS* 9183323, 2020.
- Yanga,f, Wenlu, Luib, Ronald L.M., Gaoc, Jia-Hong, Chand, Tony F., Yaub, Shing-Tung, Huang, Xudong, 2011. Independent component analysis-based classification of Alzheimer's disease MRI data. *J. Alzheimer's. Dis.: JAD, Jan. vol. 24* (4), 775–783.
- Marwa Zaabi, Nadia Smaoui, Houda Derbel, Walid Hariri. Alzheimer's disease detection using convolutional neural networks and transfer learning based methods. *17th International Multi-Conference on SSD'20*, 978–1-7281-1080-6, 2020.
- Zhang, Daoqiang, Wang, Yaping, Zhou, Luping, Yuan, Hong, Shen, Dinggang, 2011. Multimodal classification of Alzheimer's disease and mild cognitive impairment. *NeuroImage* 55, 856–867.
- Zhang, Xiaowei, Hu, Bin, Member, Ma, Xu, Xu, Linxin, 2015. Resting-state whole-brain functional connectivity networks for MCI classification using L2-regularized logistic regression (MARCH). *IEEE Trans. Nanobiosci.* VOL. 14 (NO. 2) (MARCH).
- Zhou, Ke, He, Wenguang, Xu, Yonghui, Xiong, Gangqiang, Cai, Jie, 2018. Feature selection and transfer learning for Alzheimer's disease clinical diagnosis. *Appl. Sci.* 8 (2018), 1372, 8.