International Journal of Communication Networks and Information Security

ISSN: 2073-607X, 2076-0930

Volume 14 Issue 1s Year 2022 Page 09:21

Alzheimer's And Parkinson's Disease Classification Using Deep Learning Based On MRI: A Review

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Article History

Received: 12 July 2022
Revised: 22 September 2022
Accepted: 14 October 2022

Abstract

Neurodegenerative disorders present a current challenge for accurate diagnosis and for providing precise prognostic information. Alzheimer's disease (AD) and Parkinson's disease (PD), may take several years to obtain a definitive diagnosis. Due to the increased aging population in developed countries, neurodegenerative diseases such as AD and PD have become more prevalent and thus new technologies and more accurate tests are needed to improve and accelerate the diagnostic procedure in the early stages of these diseases. Deep learning has shown significant promise in computer-assisted AD and PD diagnosis based on MRI with the widespread use of artificial intelligence in the medical domain. This article analyses and evaluates the effectiveness of existing Deep learning (DL)-based approaches to identify neurological illnesses using MRI data obtained using various modalities, including functional and structural MRI. Several current research issues are identified toward the conclusion, along with several potential future study directions.

Keywords: Deep Learning, Alzheimer's, Parkinson's, MRI, Magnetic resonance imaging

1. Introduction

Neurodegenerative diseases are one of the most alarming groups of disorders in the field of healthcare as they are unpredictable and incurable affecting mostly the aging population. They are defined by a progressive decline in the structure and function of the central nervous system mainly targeting the brain's neurons, producing aberrant growth and degeneration that ultimately results in their death [1]. Movement problems (Ataxias) and cognitive deficits (Dementias) are frequent symptoms that depend on the extent and nature of the neuronal loss. As a result, diagnosing and categorizing neurodegenerative disorders is important for clinical practice as well as for the development of effective treatments and the advancement of clinical research. The most common neurodegenerative disorders, Alzheimer's disease (AD) and Parkinson's disease (PD) are characterized by the progressive loss of function and ultimate death of neurons in the central nervous system [1]. AD is a multifaceted, degenerative neurological brain disorder. AD seems to be more prone to developing prodromal stage of AD in Mild

Cognitive Impairment (MCI), patients than in the general population [2]. Because AD starts two decades or more before symptoms are noticed, people only notice its consequences after years of brain alterations have occurred. According to Alzheimer's disease International (ADI), there are now more than 50 million dementia sufferers globally. This number is expected to rise to 152 million by 2050, which translates to one dementia case every three seconds [3].

In the substantia nigra, a particular region of the brain, dopaminergic neurons are primarily damaged by PD [4]. Since PD is a disease progressing rapidly, its symptoms gradually worsen with time. Bradykinesia, stiffness, and rest tremor are common PD symptoms that have an impact on speech, arm movements, gait, and balance [5]. At least 500,000 Americans have PD1, according to a survey from the National Institute of Environmental Health Sciences (NIEHS) [6]. Complications from PD were ranked as the 14th most frequent cause of death in the US by the Centres for Disease Control and Prevention (CDC) [7]. Most of the time, the etiology of PD is unknown. Surgery and prescription drugs are the major forms of treatment for PD because there is no known cure. Since the course of PD is quite varied, each patient will uniquely experience the disease. Various large cross-sectional demographic studies have been carried out to comprehend the underlying illness process of PD and create efficient therapies. Primarily symptoms are used to describe neurodegenerative diseases [8]. Conventional diagnostic methods are based on the medical examinations of the symptoms and thus a potential disease can be deduced based on the severity and frequency of the symptoms. However, research has shown that symptoms can be connected to a variety of illnesses and that they only partially represent the functional alterations in the affected brain regions caused by neuronal loss and altered signal transduction [9]. For instance, confusion and a decline in episodic memory are frequent symptoms of AD, MCI, and, PD in their early stages. Differential diagnosis of illnesses solely based on the symptom severity is also erroneous and inaccurate in early disease phases or atypical forms [10-12]. In the context of this, methods to evaluate changes in brain physiology were put forth to aid in the classification of neurodegenerative diseases.

Classification of medical images is a tedious and crucial task in disease diagnosis. Neuroimaging techniques that are widely used in the diagnosis of these diseases include Magnetic Resonance Imaging (MRI), Computed Tomography (CT), and Positron Emission Tomography (PET). The internal anatomy of the human body is imaged using MRI technology. The use of a rapidly varying gradient magnetic field significantly increases the speed of an MRI, improves soft tissue resolution, and causes no radiation-induced harm to the human body [13]. The feature extraction process is crucial to image classification. In conventional research, the hippocampus, amygdala, and other relevant regions of interest must be manually extracted as AD characteristics [14] and basal ganglia for PD disease [15]. Atrophy or lesions caused by these diseases can be recognized by the intensities of variation in medical images. When diagnosing AD, [16] looks at the frontotemporal lobes' atrophy. An automated diagnosis system helps greatly in clinical diagnosis. Nowadays, Neuroimaging with the advent growth of deep learning techniques has been highly effective in assessing the anatomical and functional changes of the brain [17]. The goal of this work is to review the present state of deep learning-based AD and PD detection. We particularly want to demonstrate how deep learning may be applied to increase knowledge about these diseases. To determine new findings and present trends, Deep learning-based AD and PD diagnoses are examined. The goal of this context is to examine the types of biomarkers and factors that can be used to detect diseases, the available datasets, the pre-processing methods required to deal with biological markers (notably in neuroimaging), the extraction of single features from 3D neuroimaging studies, the deep models that can capture disease-related patterns, and the handling of multimodal data.

This review paper includes three sections: i) classification of the various feature extraction and classification strategies into four main categories; ii) a review of the deep learning classification techniques used to detect these diseases, and iii) a comparative analysis based on deep learning classifying for AD and PD detection techniques. We finally conclude the review study.

2. Research Methodology

The main purpose of this review is to show how deep learning can be used to diagnose Alzheimer's and Parkinson's disease, as well as the supervised learning algorithms that have been effectively used for the segmentation and classification of MRI images of these patients. In addition, outline the advantages and disadvantages of each technique and look for ways to improve those classification techniques. As a result, existing research papers related to AD and PD detection strategies were gathered using the search engines of reputable journals: ACM, IEEE Explore, and Google Scholar databases. In primary searching, about 1000 existing articles were found based on different search queries. To improve the accuracy of the selection and retrieval procedure, instructions composed of different logic and search keywords were applied to the abstract and title. Finally, based on the segmented and extracted features that play a significant role in supervised AD and PD detection strategies, we grouped the shortlisted studies into the following primary categories:

- ROI (Region Of Interest) based feature extraction and classification techniques
- Patch-wise feature extraction and classification techniques
- Semantic or voxel-based feature extraction and classification techniques
- Slice-based feature extraction and classification techniques

3. General Approach For Diagnosing Ad And Pd With Supervised Deep Learning Techniques

Supervised DL-based techniques are a sort of machine learning that is commonly used for tasks such as early prediction, classification, and detection [18]. Because the learning method is performed using label data, they are referred to as supervised learning. DL-based models may reveal latent representations, identify correlations among distinct sections of input data images, as well as find disorder patterns using neuroimaging data [19]. Learning techniques have been effectively applied to medical scan images such as MRI (structural and functional MRI), Single-photon emission computerized tomography (SPECT), and Diffusion Tensor Imaging (DTI). The general workflow highlighting different stages for detecting AD and PD using supervised deep learning algorithms is shown in Figure 1.

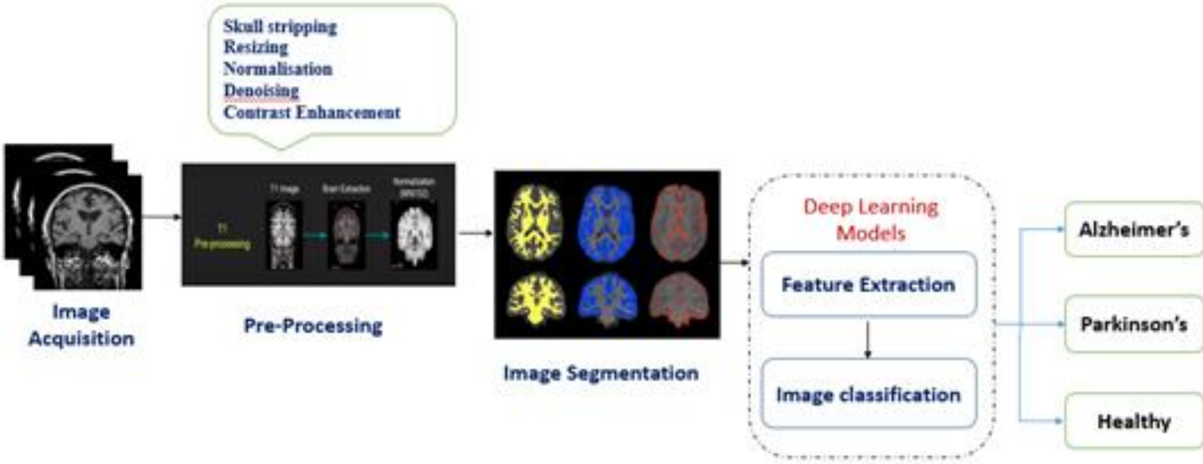

Figure 1. General Workflow Of A Typical AD And PD Classification Deep Model

As the workflow progressed, the information on the patients was loaded initially and can include demographic measures, and MRI scans (or any other neuroimaging datasets) scaled to the necessary pixel size. First, the dataset is split into training and testing datasets manually or randomly. Second, to extract feature vectors automatically, all input images are passed to the deep model. Testing data are utilized to measure the functionality of the model using previously unknown data, whereas training data are used to train the model. Finally, the performance of the model is analyzed based on different performance measures and fine-tuned accordingly to develop an efficient model.

3.1. Data Collection

The preliminary process in any supervised DL model is the collection of datasets. Many public multi-center studies tabulated in Table are available for developing clinical, neuroimaging, biochemical, and genetic biomarkers for the early prediction and prognosis of these diseases. Among these ADNI and OASIS are the benchmark datasets for most of the deep learning-based diagnosis systems for AD and PPMI for PD. Most of the PD diagnosis models are related to voice data. Here in this review, mostly MRI-based deep learning models are analyzed.

Table 1. Public Databases Of AD And PD

Dataset		**Cohorts**				
		HC	**EMCI**	**MCI**	**LMCI**	**AD**
ADNI	ADNI 1	200	-	400	-	200
	ADNI GO	200	200	400	-	200
	ADNI 2	350	300	400	150	350
	ADNI 3	483	300	551	150	437
MIRIAD		23	-	-	-	46
OASIS	OASIS-1	416 subjects and 434 MR sessions				
	OASIS-2	150 subjects and 373 MR sessions				
	OASIS-3	1098 subjects, 2168 MR sessions, 1608 PET sessions				
EPAD		2000 AD subjects				
PPMI		196 Healthy subjects, 423 idiopathic PD, 64 SWEDD				
NTUA		55 PD and 23 Normal controls 42000 images totally				

3.2 Data Preparation And Pre-Processing

Pre-processing data is a process vital for any efficient computer-aided diagnostic model. Although a deep model can perform hierarchical feature learning from raw data, it is still crucial for extracting optimal features from MRI images. Converting NIFTY or DICOM format of downloaded MRI images to either JPEG or PNG format is the first step in dataset preparation. Skull stripping, Contrast enhancement, image resizing, image registration, Normalisation, Denoising, Bias correction, and many more pre-processing methods are applied for MRI images [20].

3.3 Segmentation Approaches For Ad And Pd Diagnosis In Deep Learning

Automated diagnosis deep model algorithms can extract features automatically from the pre-processed images. Accurate and automatic brain tissue segmentation such as GM, WM, and CSF in imaging is crucial for undertaking a quantitative analysis of brain tissue volume and large-scale research of intracranial volume [21-23]. The Atlas-based method and the pattern recognition method are two important traditional approaches for segmenting brain tissues. Atlas-based techniques [24] use intensity information from an atlas to match intensity information in target images. Owing to recognition limits and variations in trustworthy actual data, strategies like atlas-based and the pattern recognition method are commonly employed for brain segmentation [23, 24]. However, they do not produce reliable findings for tiny and extremely changeable regions like the hippocampus. Tissues of the brain are categorized using a collection of pixel intensity parameters in pattern recognition algorithms [25-27]. Hippocampal atrophy has recently been postulated as a biomarker for AD[28, 29]. The hippocampus is a portion of the brain's limbic system that is surrounded by several types of tissue. A reduced hippocampus volume has been found in patients with Alzheimer's disease [30, 31]. As a result, MRI segmentation of the hippocampal region could be useful in clinical settings [32]. However, segmentation of the hippocampus in MRI is not easy because of its compact volume, partial volume impacts, structural heterogeneity, poor contrast, weak signal-to-noise ratio (SNR), uncertain edges, and closeness to the amygdala body. Moreover, manual segmentation also necessitates time-consuming professional analysis. When PD is compared to HC, there is a significant reduction in grey matter (GM) concentration with alterations in the basal ganglia region [33]. According to a recent study, traditional approaches for segmenting the hippocampus, thresholding, or region growth do not produce satisfactory results [34]. In [35] the author suggested a simple and efficient seed-based region-growing method but fails to produce impressive outcomes due to the hippocampus's indistinct edges [36].

Recently many deep learning-based models are more effective in brain segmentation to extract optimal features for classifying or predicting the stages of the diseases. Many state-of-the-art DL-based methods depend on a large amount of labeled data for training and hence complexity of computation increases. To tackle this problem, it is necessary to propose a model that performs effectively using a limited training data set. In this case, CNNs based on patches or slide windows [37-39] seem to be good where multi-size/2D/3D/multi-scale image patches of single or multi-modalities are used for segmenting ROIs (Anatomical segmentation-Hippocampus in AD/caudate nucleus in PD) or brain tissues (CSF, WM, and GM) in brain MR Images. According to this different variants of U-Net [40, 41], M-Net [42], and SegNet [43, 44] have been developed. Though SegNet is well known for semantic segmentation is not commonly employed in the segment of brain MRI images. Comparatively, the U-Net model is widely used in biomedical image segmentation as the localization is improved by the concatenation of feature maps of the encoder and decoder during up-sampling. But it cannot learn deeper features and its generalization ability is limited. The M-net model was proposed for segmenting MRI images to efficiently address these issues. [45] Proposed a SegNet model for feature extraction and Resnet101 as a classifier in the diagnosis of AD. In this paper GM, WM, cortical surface, gyri and sulci shape, cortex thickness, hippocampus, and CSF space were the seven morphological parameters recovered from the brain. To accurately and quickly segment the brain MRI scans, [46] presents a revolutionary squeeze M-SegNet (SM-SegNet) model. The suggested model uses uniform input patches, fire module's squeeze-expand convolutional layers, paired connections, and, extended skip connections to segment brain MR images. CNN's ability to self-learn allows it to outperform other methods for the same problem, resulting in a greater accuracy rate.

4. Feature Extraction And Classification For Ad And Pd Diagnosis

Features are predetermined set of qualities that may be continuous, categorical, or binary. The word "features" refer to attributes or input variables used to describe information. Getting a better data representation depends on the measures that are available and is domain-specific. Extracted features can be viewed as a simple procedure for reducing the dimensionality of data. Direct classification is challenging due to the original image's size and noise. However, Deep Learning models can extract features automatically. According to the type of collected features, the source data processing method may be split into five different categories: ROI-based, patch-based, semantic-wise or voxel-based, and Slice-based.

4.1 ROI-Based

The measurement of region value is calculated as a feature of age classification, and the ROI feature is created by grouping voxels from the modified given atlas. Rather than examining the entire brain, the ROI approach concentrates on specific parts of the brain that are known to be impacted early in AD or PD. To classify AD or PD, deep learning networks can be employed to extract prospective features from ROI measurements of various imaging models. Suk et al proposed a Deep Auto Encoder model to extract hierarchical and nonlinear relationships among ROIs from resting state fMRI images to classify AD in healthy patients. The author [47] obtained 93 volumetric deep ROI features as well as CSF biomarkers from PET and MRI scan images and then utilized a linear orthogonal transformation approach called principal component analysis (PCA) to retrieve an optimal subset of features in the multiclass AD classification. The paper [48] extracted ROI features by combining both patch-based GM features and the deformation amplitude of MRI scans. [49] extracted ROI features from PET images with the use of a deep learning model. A deep model [50] is proposed to classify healthy and PD patients based on ROI features from subject-level MRI slices. [51] used a deep model to classify PD based on ROI-based features from SPECT images. Morphological abnormalities produced by neurodegenerative disorders may not necessarily occur in designated ROIs and may include several ROIs or partially retrieved ROIs. As a result, this technique's implementation does not produce stable performance.

4.2 Patch-Based

Local regions rather than the entire brain or individual voxels experience modifications in the early stages of the disease. The patch-based approach can discover diseases in the brain by feature extraction from small patches. The key issue with the patch-based strategy is selecting the much more useful picture patches capturing both local and worldwide information. Specifically based on left and right hippocampus regions in sMRI, a patch-based approach [52] incorporated an ensemble of CNNs as feature extractors and softmax classifier for AD classification. The paper [53] classified AD categories based on different patch sizes of FDG-PET images. Transfer learning is proposed by [54] in which a CNN-based deep model is used to retrieve optimal hyperparameters from MR image patches to classify PD. [55] compared the efficiency of two anomalous detection models based on the spatial autoencoder and the patch-based Siamese autoencoder in the detection of PD. The Siamese autoencoder model performs better on average, indicating that the patch-fed networking model may be useful.

4.3 Semantic-Based Or Voxel-Based

The easiest analysis method is the voxel-based approach. They make use of the Grey Matter/White Matter/Cerebro Spinal Fluid in MRI images as well as pixel intensity values from the whole neuroimaging modalities. This method often needs image registration, which involves standardizing the individual brain pictures to a common three-dimensional space. About 70% of the research in this category carried either a single-modality or multi-modality full-brain imaging analysis. However, before using a deep model on MRI images, tissue segmentation was carried out in the remaining studies. Since they only examine a portion of the brain, tissue segmentation based on voxels cannot be regarded as an analysis of a whole-brain image. A feature-based dimension reduction approach is usually used in voxel-based machine learning methods, however, deep structures may not gain from this. However, a voxel initial selection method can be utilized for every brain imaging modality separately to address high feature dimensionality. For instance, in [56] GM images divided into 3D patches based on the Automated Anatomical Labeling (AAL) atlas regions were used to train various deep belief networks and different voting schemes were used for the final prediction. In [57] the author proposed voxel-based morphometry on MRI images for the PD classification to analyze the thickness of grey matter where depletion of nerve cells that generate dopamine occurs.

4.4 Slice-Based

Slice-based frameworks consider that some intriguing characteristics can be represented in 2D pictures, which reduces the overall number of hyper-parameters. While some research studies use standard neuroimaging projections like the frontal plane (coronal), horizontal plane (axial), and median plane(sagittal), others use a unique method to create 2D slices from a 3D image of a brain scan. Although 2D slices cannot contain all the data of a brain, neither of the papers in this group examined the whole brain regions. Slice-based approaches often include the center part of the brain and disregard the remainder in contrast to using tissue segmentation. The most popular view is axial projection. For instance, [58]. used horizontal projections i.e., axial view of GM volumes, discarding the beginning and ending slices since they are empty of data. In other instances, median axial MRI slices [59], 166 axial planes of GM slices [60], and 43 axial fMRI slices [61] have been employed. In the two investigations [62, 63], GM was created by concatenating all other slices, except the final 10 axial slices and slices, having zero mean pixels for each person. An automated diagnosis CNN-based model [64] incorporated the mid-brain T2-weighted MRI slices of PD and healthy controls. [50] demonstrated the generalized performance of the two cutting-edge pre-trained deep CNN-based models (VGG 16 and ResNet 50) by splitting MRI slices in two different ways one at the subject level and the other by combining all the slices to make training and test datasets to classify AD, PD, and Healthy controls.

5 . Comparative Analysis Of Detection Techniques, Issues, And Possible Solutions

Different feature extraction techniques have their benefits and drawbacks. The voxel-based approach is the objective analytical technique that normally processes the brain consistently without changing its morphology [66]. But it disregards local information and as it involves a lot of voxels, the voxel preselection method is essential. Although the network can be made simpler and fewer training parameters can be generated by using 2D slices as input, the spatial correlation between nearby slices will be lost. Coronal and sagittal projections of the slice approaches are more recognizable, but axial projections are the most popular ones. Brain scanning will be more or less influenced by noises, typically caused by the patient's neural activity, equipment environment, operators, etc. There is a lot of data available from brain imaging. Extraction of representative regions is required for effective picture classification. The ROI-based approach is simple to understand and can be applied in healthcare settings, and the entire nervous system can be expressed using limited attributes [67]. The feature size is consequently less compared to that of the voxel-based and slice-based approaches. According to research studies, grey matter volume, the hippocampus, cortical thickness, substantia nigra, and other specific areas of the brain can all be effectively used as ROI. The distribution of disordered brain areas contains numerous unidentified regions, which may cause information loss and restrict the capacity to identify features. Conversely, the feature extraction method based on patches is more accurate and does not require ROI detection.

Also, the quality of neuroimaging is very important in the classification of these diseases. Combining neuroimaging features with other biomarkers like genetic data, CSF analysis, cognitive scores, and rating scales (MMSE, UPDRS) can improve the accuracy of classification [86]. From the recent papers, it is clear that most of the research employs CNN-based models for medical image analysis. But they require large data for training and more powerful graphics processing units with a longer time for training. The general solutions to this problem are data augmentation and employing pre-trained models i.e., transfer learning. Many recent research studies have proposed the concept of transfer learning and achieved significantly better accuracy. 3D CNN models are also popular nowadays for the diagnosis of AD and PD.

Table 2. Deep Learning Applications In Alzheimer's Disease Diagnosis

Ref/Year	Approach	Dataset	Deep learning models	Accuracy
[70]/2016	Voxel-based	ADNI and CADDementia-MRI samples	CAE and Adaptable 3D CNN	94.8%
[69]/2017	ROI-based	ADNI-MRI samples and clinical data	CNN with residual blocks	86.4%
[72]/2017	ROI-based	ADNI-MRI data	Transfer learning	93.4%
[71]/2019	Slice-based	ADNI and Milan hospital dataset	CNN	99.2%
[74]/2020	Slice-based	OASIS+MIRIAD-MRI	2D CNN	82%
[76]/2020	Slice-based	OASIS-MRI	Siamese CNN model (VGG16)	99.05%
[78]/2020	Patch-based	ADNI-MRI	3D DenseNet	88.9%
[73]/2021	ROI-based	ADNI-MRI, clinical and genetic data	3D CNN	84%
[75]/2021	ROI-based	ADNI-MRI	Deep CNN	96%
[77]/2021	Slice-based	OASIS-MRI	Transfer learning (AlexNet)	99.2%
[68]/2022	Slice-based	ADNI-sMRI coronal grey matter slices	ResNet with a regional attention mechanism	90%

Table 3. Deep Learning Applications In Parkinson's Disease Diagnosis

Ref/Year	Approach	Dataset	Deep learning models	Accuracy
[64]/2018	Slice-based + ROI- based	PPMI-MRI	2D CNN	96%
[6]/2018	ROI-based	PPMI-DTI images	Multi-view Graph Convolutional neural network (MVCGN)	AUC-0.9537
[81]/2020	Slice-based	PPMI and Greece hospital 3D MRI triplets & DaTscans	Deep convolutional and recurrent neural network	98%
[82]/2020	ROI-based	PPMI-MRI	Ensemble learning	94.7%
[84]/2020	ROI-based	PPMI-DaT scans	Transfer learning (VGG16)	95.2%
[55]/2021	Patch-based	PPMI-MRI	spatial auto-encoder (AE) & patch-fed Siamese auto-encoder (SAE)	g-mean 66.9%
[79]/2021	Slice-based	NTUA-MRI	DenseNet-LSTM	93.8%
[85]/2022	ROI-based	PPMI-resting state fMRI data	LSTM	71.63%

The convolutional layers in CNN struggle to accurately extract the correlation with the far pixels in the feature space. An attention mechanism is implemented to enable the system to disregard insignificant data and concentrate on crucial data while learning the link between features [68]. It has significantly developed in recent years. The Spatial Transformer Networks model (STN) [81], Squeeze-and-Excitation model (SE) [83], and convolutional block attention model [65] are some of the recent attention-based models used recently to improve the efficiency of the DL architectures. Further rapid advances in graph-based network architectures like graph convolutional neural networks (GCNs) have gained insights into the area of healthcare image analysis with the advancement of diagnosis and disease stage prediction. An overview of the contributions of different deep learning-based models for the classification of AD and PD is tabulated in Table 2 and Table 3.

6. Conclusion

From the above discussion, it is clear that deep learning-based models have become more effective in medical image analysis. Owing to their nature of automatic feature extraction, they have achieved superior performance over traditional machine learning algorithms in predicting AD and PD. This paper has explored the most popular recent deep learning techniques and their advancements in the detection of these diseases. Different approaches to various feature extraction and classification methods using deep learning techniques with their pros and cons have been discussed. Also, the comparative analysis of these techniques based on their performance has been summarised. Owing to pre-processing, registration to a common anatomical space and intensity normalization are advised. Due to their capacity to include specific disease-related characteristics, ROI-based and patch-based approaches for MRI image handling have indeed been claimed to be much more effective than voxel-based and slice-based ones. In this study, numerous deep models have been discussed. Regarding the classification approach, CNNs have been more frequently used than other deep models and are reported to have better accuracy in this area. An autonomous multi-modal longitudinal method is preferred as the ultimate goal for an AD and PD detection system. But apart from the final detection solution, dataset overfitting issues due to limited data still need to be addressed. Alternate solutions of incorporating transfer learning, data augmentation, attention, and transformers-based deep models, and an ensemble of cutting-edge machine learning techniques with deep learning models have to be revised further in the future.

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