A SURVEY ON AI-BASED PARKINSON DISEASE DETECTION: TAXONOMY, CASE STUDY, AND RESEARCH CHALLENGES

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Abstract. Parkinson Disease (PD) is most common diseases from majority of disease encountered all over the world, with more than 7 million individuals being affected. PD is a type of progressive nervous system disease, causing deterioration in health or function. The timely identification of PD is a significant challenge because it rarely shows symptoms in the early stages. Moreover, it is typically encountered in older people where the symptoms sometimes coincide with age-related issues. Deep Learning (DL) can be integrated into many methodologies in diagnosing PD, such as Magnetic Resonance Imaging (MRI) and Single-Photon Emission Computed Tomography (SPECT). DL algorithms can detect PD based on observing some common symptoms. Moreover, it can also be detected using brain MRI images. So, in this study, we reviewed existing DL algorithms for timely identification of PD. We also have developed a CNN model for the timely identification of PD. We used 3D brain MRI images of PPMI datasets and achieved the 88% accuracy.

Key words: PD, DL, MRI, Pre-processing, Datasets

1. Introduction. Parkinson's Disease (PD) is one of the most frequent worldwide diseases. According to the World Health Organisation (WHO), 7-10 million individuals are diagnosed with PD. In PD patients, men and women are in the ratio of 3:2, and people above the age of fifty develop PD in general [33]. In human brain, Dopamine sends messages between brain cells so that human body motions remain flexible and synchronised [28]. Certain parts of the human brain include dopamine-producing cells. The SN area of the brain contains a high density of these cells. When these cells are destroyed or under-operated, PD symptoms develop. The cause of these neuron disorders is currently unknown. PD is a progressive type of disease of the nervous system. A progressive disease worsens with time, resulting in deterioration in health or function. Insufficient dopamine production leads to muscle tremors, stiffness, and slowdown. A loss in scent sensitivity, muscle tremors while at rest, bending of the body posture, numbness, tingling, discomfort in the limbs, sleep difficulties, constipation, and slow movements are common symptoms in PD [58].

The early detection of PD is challenging for various reasons. Motor symptoms have traditionally been utilised to make the diagnosis of PD. The majority of patients with this disease are above the age of sixty, making it time-consuming and uncomfortable for them to have repeated scans and for neurologists and other specialists in movement disorders to diagnose the condition [11]. To diagnose and measure the severity of PD, medical professionals may use various Radiological Imaging (RI) Studies of the human brain. Some of them are Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), Single-Photon Emission Computed Tomography (SPECT), Structural Magnetic Resonance Imaging (sMRI), Diffusion Tensor Imaging (DTI), etc.

Various RI Studies are crucial in diagnosing and managing PD. These imaging techniques provide essential insights into the anatomical and functional changes taking place in PD patients' brains, allowing for a more accurate diagnosis and aiding in disease progression monitoring. MRI is frequently used as the first-line imaging technique for diagnosing PD. It provides comprehensive structural images of the brain, which can help rule out

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Table 1.1: Commonly used abbreviations

Acronym	Abbreviations
PD	Parkinson's Disease
DL	Deep Learning
MRI	Magnetic Resonance Imaging
SPECT	Single-Photon Emission Computed Tomography
CNN	Convolutional Neural Network
PPMI	Parkinson's Progression Markers Initiative
SN	Substantia Nigra
PET	Positron Emission Tomography
DTI	Diffusion Tensor Imaging
DaT	Dopamine Active Transporter
fMRI	Functional MRI
AI	Artificial Intelligence
sMRI	Structural MRI
HC	Healthy Controls
CNNs	Computational Neural Networks
ANN	Artificial Neural networks
CR-ML	Contrast Ratio classifier
RA-ML	Radiomics based classifier

other potential explanations of comparable symptoms, and it can reveal shrinkage of the brain or abnormalities in specific regions, such as the Substantia nigra (SN), which is frequently afflicted in PD. Dopamine Active Transporter (DaT) scan, an example of SPECT, is very useful in diagnosing PD. It assesses the density of dopamine transporters in the basal ganglia, where dopamine insufficiency is a characteristic of PD. Reduced dopamine transporter binding in this area is an important diagnostic marker. PET scans provide dynamic information regarding brain function, such as glucose metabolism and dopamine levels. PET scans can distinguish PD from other movement disorders and follow disease progression, which aids in therapy planning. Functional Magnetic Resonance Imaging (fMRI) measures brain activity and connectivity to detect changes during the disease [10]. Khan *et al.* [30] discussed the use of brain anatomical MRI for diagnostic classification of Alzheimer's disease, which signifies the potential of neuroimaging techniques, such as functional MRI, while examining neurodegenerative diseases like Parkinson's disease.

It enables researchers and physicians to better understand how PD affects different brain regions, offering information on how the disease affects cognition and non-motor symptoms. These scans allow clinicians to make informed treatment decisions and provide vital insights into the evolving nature of the disease, ultimately increasing the quality of care for those living with PD.

The physicians who analyse the patient's data and symptoms must have a thorough understanding of the disease. Unfortunately, many countries do not have enough qualified doctors. As a result, identifying or detecting PD is a difficult process because specialists are stressed as a result of their job. Doctors can describe medications, but they lose effectiveness as the disease worsens from its early stages. As a result, early detection of Parkinson's disease is critical for taking immediate steps to assist people preserve their independence for as long as possible. This explanation has prompted healthcare providers to develop a decision support system based on computer aided diagnosis to assist clinicians in diagnosing PD [35]. This method can serve as a second opinion for PD diagnosis while lowering the likelihood of errors due to the use of Artificial Intelligence (AI) and Deep Learning (DL). [17]

DL also enables the integration of many radiological methodologies, such as MRI and SPECT, in diagnosing PD. By using DL algorithms to identify crucial traits that are typically not used in the clinical diagnosis of PD, we may be able to detect PD in preclinical stages or atypical forms. DL models are increasingly used for early PD detection because they detect minute patterns in Radiological Imaging (RI) data. PD frequently manifests subtle symptoms that are difficult to diagnose ordinarily. DL's ability to analyse varied data sources,

such as medical imaging and patient records, aids in identifying early markers and biomarkers. This allows for earlier detection and more effective therapies. These models enable unbiased, dependable data analysis while minimising human errors and biases. They are critical for improving the detection of PD and treatment because of their ability to provide personalised assessments, follow disease progression, and assist ongoing research.

Weng *et al.* [65] used SPECT imaging for diagnosing PD with 99m Tc-TRODAT-1, discusses the age-related depletion in the striatal binding in both PD patients as well as Healthy patients. and concluded that 99mTc-TRODAT-1 SPECT imaging is a helpful and remarkable diagnostic tool for clinical applications in determining the decrease of striatal DAT concentration in PD patients. Bae *et al.* [5] presented some imaging techniques used in PD and other Parkinsonian syndromes. The nigral structure includes markers to help complex neuroimaging procedures using MRI to find pathophysiologic, functional, and neuroanatomical changes. These markers can help diagnose the subtype, monitor disease severity of PD and separate PD from other movement disorders. Noor *et al.* [40] used the model that is based on 3D separable and grouped convolutions to highlight fine-grained descriptive features from sMRI and attained the accuracy of 86% with sensitivity of 87.5% and specificity of 85.7%. Chen *et al.* [14] seeking to develop a model that relies on intra/intervoxel metrics derived from DTI to facilitate automatic differentiation of PD patients without dementia into Mild Cognitive Impairment (MCI) and Normal cognition groups (NC).

This paper mainly focuses on various structural changes in PD and its symptoms. Further, different types of datasets, multiple types of data preprocessing technique which is commonly used and some implemented DL models for early detection of PD are also covered. Moreover, to support the above discussion, one case study is included with the Convolutional Neural Network (CNN) model executed on 3D brain MRI images with 88% accuracy.

1.1. Research Contributions. The significant research contributions are listed as follows:
- We have discussed pathology, symptoms, and treatment of the Parkinson Disease along with the on brief description on symptoms and causes of the same.
- We have gone through different datasets followed by various data pre-processing methods, extended by DL algorithms for the early diagnosis of PD.
- We have implemented CNN model in our case study to diagnose Parkinson's disease using 3D-MRI from the Parkinson's progression markers Initiative (PPMI) dataset. The model 88% accuracy in predicting the disease.
- At the end we have elaborated the research challenges and future scopes of researches in this domain .

1.2. Article Layout. The rest of the paper is as follows. Section 2 discusses the fundamental aspects of PD with some commonly observed symptoms. Section 3 gives the overview of the different datasets, various data preprocessing techniques and different DL models, some people applied in the past. Section 4 includes implementing the CNN model on 3D brain MRI images. Section 5 discusses the analysis of performance achieved by the CNN model. Challenges after and before using the DL model for early diagnosing PD are discussed in section 6. Finally, the paper is concluded in section 7.

1.3. Scope of the survey. Gilat *et al.* [25] assessed the brain activity related to body movement. Gain impairment is the primary disability shown in PD. Even when PD is in the early stage, patients often experience this disability and gait problems can cause other physical issues, leading to severe injuries, immobilisation and mortality. They have reviewed the articles that used PET, SPECT or fMRI, which examined the neurological mechanisms behind gait impairment in PD patients. However, they have only included studies that model gait in PD patients.

Bharti *et al.* [9] discussed existing research studies on structural and functional neuroimaging studies in PD and provided an overview of knowledge regarding Freezing of Gait (FOG) condition. FOG is typically seen in later stages of PD and is generally resistant to medicinal treatment. It contributes to a severe decline in quality of life. They have considered MRI, fMRI, SPECT and PET for brain changes in FOG condition of PD.

Wang *et al.* [63] assessed the diagnostic utility of Neuromelanin sensitive MRI (NMS-MRI) in PD using a meta-analysis technique. They focused on research that examined the Substantia nigra pars compacta (SNpc) structure's signal strength, volume, or area as well as the precise sensitivity and specificity of the cutoff value in order to identify PD.

Cho *et al.* [15] also looked at research on NeuroMelanin-sensitive (NMS-MRI) of clinically diagnosed PD patients or Healthy Controls (HC). They evaluated the diagnostic effectiveness of NeuroMelanin-sensitive (NMS-MRI) for differentiating HC from patients with PD and discovered variables causing heterogeneity, which had an impact on the diagnostic effectiveness of this method across studies. They did not, however, concentrate on the patients' further radiological scans or various MRI variations.

Bergamino *et al.* [6] concentrated on improvements in DTI methodology and only looked at diffusion weighted magnetic resonance imaging (dMRI) tests in early-stage PD. It has been demonstrated that these cutting-edge techniques can identify structural White matter (WM) abnormalities in PD in its early stages. The method most commonly used to examine WM pathological alterations in symptomatic regions like the SN is DTI.

Alzubaidi *et al.* [3] summarised the research studies that contained DL techniques introduced or developed to diagnose PD. They also set some limitations on the types of publications and the research language. Peer-reviewed papers, conference proceedings, reports, theses, and dissertations in English were the only ones approved. They looked into the use of neural network algorithms, notably DL algorithms, for the early detection of PD but did not provide a full evaluation of its quality.

Feraco *et al.* [24] assessed articles containing modern MRI techniques for studying the SN to aid in diagnosing and treating PD. In their research, they used Nigrosome imaging, Neuromelanin sensitive sequences, iron-sensitive sequences, and improved dMRI to characterise SN damage in PD better. These approaches are emerging as promising early diagnostic biomarkers for PD.

Inspired by this, we prepared an exhaustive and comprehensive survey on PD detection that can help medical practitioners and researcher working in the same domain. The survey comprises of fundamental aspects of PD, symptoms, conventional detection mechanism, and its challenges. Further, we presented a thorough taxonomy that shows the AI-based PD detection mechanisms. In addition, a case study has been proposed where AI techniques are used to detect PD to showcase the competency of AI in healthcare domain. Lastly, we highlighted the research challenges that still hinder the performance of PD detection.

2. Background. The section includes the functional aspects of PD, some of its common reasons, its symptoms, some DL model and concludes with current curing methods. The detailed description is as follows.

PD is a complex neurodegenerative disorganisation that seeds unexpected or uncontrolled motions such as shaking, stiffness and unsteadiness and coordination, and the symptoms may worsen over time, which involves a small, dark-colored portion of the brain called the SN. This is a significant production ground for dopamine in the brain. Dopamine is the chemical released in the brain that acts as messenger and transmits messages between nerves, which controls muscle movements, including those of the brain's pleasure and reward centres.

A distinctive trait of PD is the aggregation of exceptional protein known as Lewy bodies in specific brain cells, including dopamine-producing neurons. These Lewy bodies mainly consist of misfolded alpha-synuclein protein. The presence of Lewy bodies intrudes cellular function and facilitates neuronal dysfunction and eventual cell death. Inflammation within the brain, commonly known as neuroinflammation, plays a role in improving PD. The activated immune cells and inflammatory molecules can cause damage to the neurons and even escalate the disease process. Mitochondria, commonly known as the powerhouse of the cells, plays a vital role in maintaining cell health. Dysfunction in mitochondria can lead to oxidative stress and impaired energy production. Oxidative stress, which, in turn, can harm neurons and even cause degeneration. PD can affect the normal secretion of abnormal proteins, including alpha-synuclein, which accumulates protein aggregation, contributing to rupture or damage to the ultimate neural system.

Neurons depend on the effective transport system to move essential molecules along their long axons. The damage caused by PD on the nervous system weakens the delivery process of nutrients and signalling molecules, leading to cell dysfunction and death. The basal ganglia, the part of or the region in the brain which controls the movements, includes motor symptoms that are motor learning. PD mainly affects this part, and the signs are evident when the nerve cells in the basal ganglia become harmed or die. These nerve cells commonly produce a vital brain chemical fluid known as dopamine, so when they are dead, the source of dopamine production becomes less, resulting in movement problems associated with the disease. Reported cases of PD can be connected with specific genetic variants, while some cases are inherited from blood. However, PD is mainly known to have genetic grounds, and the condition is scarcely found in families. Copious experts have
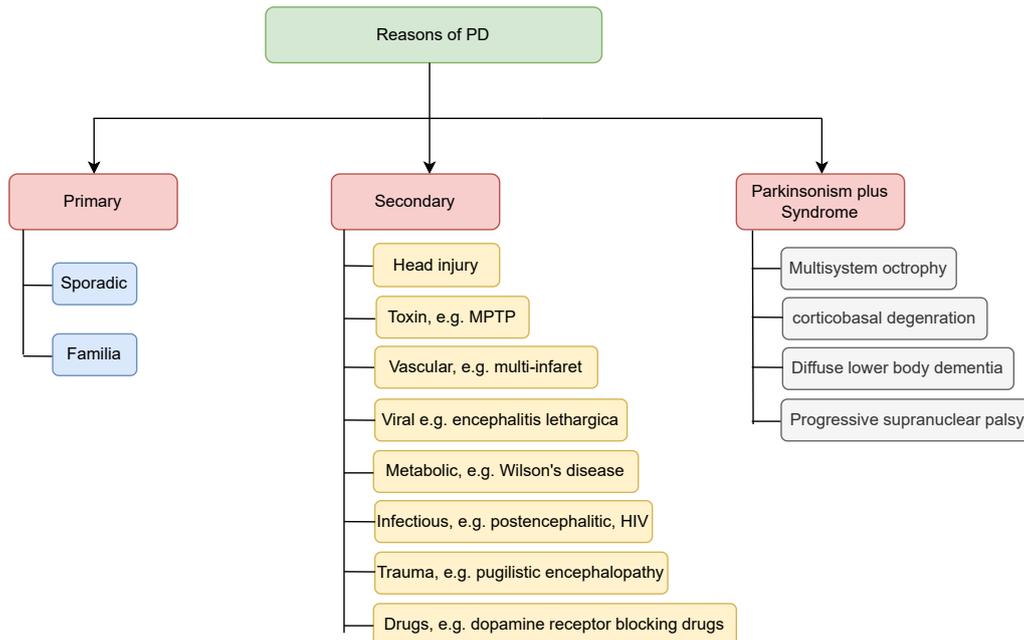
Fig. 2.1: Causes of PD

now concluded that genetic and environmental factors, including exposure to harmful chemicals, commonly contribute to the cause of PD. Some of the reasons are classified below:

- Primary: The primary reason for PD can be sporadic, which means it is a chronic progressive disorder in which idiopathic PD occur without substantial evidence. The other primary reason is Genetics, which may occur from single genes.
- Secondary: The cause of PD is reduction in dopamine level. The reason for the reduction of dopamine level can be toxins like MPTP(1-methyl 4-phenyl tetrahydropyridine), viral-like encephalitis lethargica, metabolic like Wilson disease, head injury, infectious like postencephalitic, drugs like dopamine receptors blocking drugs, vascular like multi-infact, trauma, etc.
- Parkinsonism plus syndrome: This syndrome can have various types which are multisystem octrophy, corticobasal degeneration, diffuse lower body dementia and progressive supranuclear palsy
- Environmental Factors: Sometimes, there are chances of PD in people of rural areas due to drinking well water, high pesticide exposure, oxidative stress, etc.

The Fig. 2.1 gives the overview of the following causes of PD.

The general estimation says that when almost 80 percent of the dopaminergic cells are lost before the motor symptoms are observed. The degradation of the nigrostriatal dopaminergic system is observed when there is a erosion of more than 70% of the striatum's dopamine and more than 50% erosion of dopaminergic neurons in SN [59]. So early PD detection is sometimes miscellaneous task. Therefore for PD detection some rules or criteria are proposed from the United Kingdom Brain Bank [54]. The below mentioned are criteria are as follows [20]:

- Diagnose of Parkinson's syndrome: When Parkinson is at the initial stages, it can be generally identified with a reduction in movement speed and other day-to-day activities, also known as Bradykinesia [39]. Other symptoms that can be observed are rigidness in muscles, rest tremors of 4 - 6 Hz frequency and sometimes posture instability, which cannot be generally observed at the initial stages.
- Exclusion criteria for PD: Some exclusion symptoms cannot be detected as the PD, though they are present. They are Parkinson's symptoms, which gradually increase after a history of multiple strokes, numerous head traumas in the past, Oculogyric crises, definite encephalitis in the past, beginning of

Table 2.1: Motor and non-motor symptoms of PD

Motor Symptoms	Non Motor Symptoms
Bradykinesia	Anosmia
Rest tremor	overtiredness
Rigidity	Low Blood pressure or hypotension
Falls & Dizziness	Bladder & Bowl problems
Freezing	Restless legs
Muscle cramps	Skin & perspiring problems
Micrographia	Speech & communication problem
Masked facies	Eye ailments
Reduced eye blinking	Pain
Drooling	Anxiety
Soft voice	Depression
Dysphagia	Hallucinations & delusions

neuroleptic therapy for symptoms, more than one affected relative, sustained remission, Strictly unilateral features after three years, supranuclear gaze palsy, Cerebellar signs, early severe autonomic involvement, early severe dementia with memory, language, and practical difficulties, Babinski sign, CT(Computerized Tomography) scan showing the presence of a brain tumour or communicating hydrocephalus, negative response to large doses of Levodopa (if malabsorption excluded), MPTP(1-methyl 4-phenyl tetrahydropyridine) exposure.

- Supportive criteria for PD: The criteria in support of the PD are unilateral onset, presence of rest tremor, progressive disorder, continuous asymmetry, which the onset side has the most effect, positive feedback to levodopa drug, severe levodopa-induced chorea, Levodopa response for five years or more, clinical course of 10 years or more.

Based on the above criteria, it can be generally concluded whether the patient has PD. Moving further, PD also shows many symptoms. These symptoms are divided into two broad categories, which further narrow down. Table 2.1 summarizes this symptoms. These broad classifications of the symptoms are as follows:

- Motor Symptoms
- Non-Motor Symptoms

2.1. Motor Symptoms. The symptoms which cause an effect on the movement and balance are known as motor symptoms. The UPDRS(Unified parkinson disease rating scale) score helps in identifying the extent to which the disease can affect [66]. Other people with naked eyes can easily observe these symptoms. Some of them are shown here.

- Tremor: This is an early-stage symptom that is observed in 70% people of the PD. The tremor means the shaking of body parts with frequency of around 4 - 6 Hz. This is most prominent at rest and worsens with emotional stress. Generally, this starts with rhythmic flexion-extension of the finger, hand, and foot or with rhythmic inward-outward forearm rotation. This is not observed during voluntary movement and sleep. At an early stage, this symptom is limited to a limb or two limbs on same side before being generalised. It can be observed in the jaw and chin but not in the head [68].
- Rigidity: It means an increase in resistance against the passive movement of the body parts, which leads to stiffness and flexed posture. This is more a sign rather than a symptom. The stiffness on the languid limb can be defined as the lead pipe rigidity, as the muscle tone is present in the whole limb's movement. When tremors coincide with rigidity, there is a feeling of ratchet-like jerkiness, known as cogwheel rigidity [4].
- Postural changes: There is a stooped body posture due to PD. This is because of the rigidity which forces the body to lean on one side. Moreover, the PD harms the automatic activities of brain, leading to stooped posture as the brain is not commanding to stand straight. This reduces body movement and functional capacity [22].

- Gait changes: The gait means walking pattern. Due to PD, there is a significant change in gait pattern, like slow turns, reduced arm movement, slow stumble, reduced blinking of the eyes, chances of falling forward, and small stride length in walking.
- Speech and Swallowing: People with PD may suffer from chewing or eating difficulties, increased salivation in the mouth, and garble.
- Changing in writing patterns: A test is performed on the patient in which the patient has to write some sentences or draw the spiral on paper. Then, based on the frequency of vibration of hands, which can be observed by seeing the work, the doctor gets more clarity on PD detection.[56]

2.2. Non-Motor Symptoms. The symptoms that are not associated with movement and balance are known as non-motor symptoms. Other people with naked eyes cannot easily observe these symptoms. Non-motor features can early than the motor clinical features, which are increasingly recognised as important features during the phase of pre-PD. Some of them are discussed here:

- Eye problems: One common issue PD patients face is eyesight problems. But it is not entirely related to PD; many other factors can affect eyesight or cause eyesight issues. PD patients may face relatively high issues when moving their eyes or trying to force them quickly. This might be more evident when looking at fast-moving objects like vehicles. This problem can also be caused by Progressive Supranuclear Palsy (PSP), which has symptoms similar to PD. Taking the medicine for PD, particularly anticholinergics, can result in blurred vision. Patients might see double images of a single object simultaneously. Poor coordination and wearouts of the muscles that move the eyeballs mean that the eyes have trouble moving together, causing double vision. Other problems, such as diabetes, can also cause double vision. Other eye problems that PD patients may feel are dry eyes, eyelid apraxia, contrast sensitivity, Colour vision problems, difficulty measuring space, etc [37].
- Depression: Depression might increase or lower mood and emotional health. Some of the problems that a depressed person experiences are difficulty concentrating, tiredness, lack of sleep or excessive sleep, loss of appetite or increased appetite, the expertise of worthlessness or guilt. In most critical cases, thoughts of death or self-harm and suicidal ideas can be the symptoms due to lack of dopamine [49].
- Fatigue: Fatigue can be expressed as an overwhelming feeling of tiredness, exhaustion and a lack of energy. Often, tiredness and fatigue are misunderstood. Tiredness usually goes away with a good nap or rest. But with fatigue, it does not improve with rest. Up to half of the PD patients experience fatigue. Fatigue might not be related to PD but could be caused by another condition like a thyroid problem.
- Anxiety: Anxiety is a state of nervousness characterised by worry or fear. If they find it difficult to face a situation, everyone in their lives exhibits anxiousness. A sense of imminent danger, constant worry, trouble focusing, an inability to relax, trouble sleeping, sweating, a racing heart, tightness in the chest, dizziness, trembling, nausea, stomach aches, appetite loss, a dry mouth, muscle pain, tension, restless legs, difficulty getting a good night's sleep, etc. are some of the symptoms that an anxious person may experience. Your daily life may be impacted if these sensations persist for an extended amount of time. Anxiety and sadness symptoms are sometimes present in patients. Although there may be overlap, there are three primary categories of anxiety. Multiple types may be experienced by many patients.
  1. Generalised Anxiety Disorder
  2. Panic attacks
  3. Phobia

For people with and without PD, anxiety is probably caused by a combination of several things, including genetics and stressful daily life.
- Skin and sweating: Daily-life PD patients are mainly affected. The skin has glands that produce a greasy/oily substance called sebaceous matter, known as sebum. The production of sebum in PD patients is more than that of non-PD patients. This means the skin, especially the face and scalp, becomes greasy and shiny. They may suffer from seborrhoeic dermatitis. In this, the areas of the skin that consist of sebaceous glands become red and itchy. This is also a common occurrence and can happen without PD. Thus, these conditions in PD patients can be in the scalp, face, ears, chest, bends

and folds of skin like under the arms. And this is not caused by poor personal hygiene. PD patients can experience extreme sweating (hyperhidrosis). This happens if the prescribed medications lose their effects at the end of their dose. This can also occur when the drugs are working at their best. Some patients with PD may not sweat enough. This is called hypohidrosis. This may be a side effect of anticholinergics, a medication used to treat PD.

Another rarely used classification is through the sensory symptoms, including the gradual loss of smell, which can be detected by the University of Pennsylvania Smell Identification Test (UPSIT) [36]. Generally, the peripheral sensory symptoms like smell start to affect more early. This loss in smell symptoms is seen even earlier than motor or non-motor symptoms. This loss in smell is observed in around 75 to 95 percent of PD people. But for the taste sensor, it is followed. Generally, the taste loss is observed in the advanced stage, but in rare cases, the loss of taste can be observed earlier [41]. Moreover, impairment in voice is also observed as one of the common symptoms in many PD patients [2].

The above discussed are the symptoms that are in support of the PD. As discussed earlier, many of these symptoms are observed near the last stage. But to get the early detection of PD based on brain MRI, various DL models can be used, one of which is CNN, discussed below.

The CNN is a type of DL neural network architecture that is commonly used for applications in image and speech interpretation. High dimensionality of images can be filtered by convolutional layers that basically extracts features and store in matrix-grid structure without compromising with its informational data. That is why CNNs are especially suited for this image classification. Layers in CNN: a input layer, a convolutional layer, a pooling layer, flattening, a fully connected layer and a output layer. vasquez *et al.* [61] came up with an approach to model such difficulties in starting or in stopping movements taking into account the information from speech, handwriting, and gait. They used those adaptions to train CNN to classify patients and healthy subjects. Once the model finally detects the PD, the final step is to cure the same. But currently, no treatments are available that can completely cure it as it is impossible to reverse the degeneration of neurons that causes PD. However, many treatments can help your symptoms. Treatments for Parkinson's include:

- Surgical: It includes Deep Brain Stimulus, a neurosurgical technique for curing PD. It uses embedded electrodes and electrical stimulation to cure the disorder related to the movement of neurons inside the brain. In this process, external electric currents stimulate the brain cells. This current is supplied by the device kept near the clavicle [19].
- Drug-oriented: The drugs-oriented method can be chosen to get temporary relief against PD. Two drugs are commonly used, which are levodopa and carbidopa intestinal gel. The levodopa drug provides dopamine to the brain, which is deficient in PD patients. The carbidopa, a peripheral L-dopa decarboxylase inhabitor drug, ensures that the levodopa drug only increases the dopamine level of the brain as there are many sources of dopamine in our body[45].

The social and economic environment might influence treatment decisions, such as when to begin therapy, what sorts of treatment to utilise, and whether to change treatment. As the medical condition changes, treatment may need to be adjusted on a frequent basis to balance quality-of-life concerns, treatment side effects, and treatment expenses. A regular checkup with members of your healthcare team is required to adapt your therapy as your condition evolves.

Imaging can be helpful in patients with uncertainty in diagnosis (e.g., early stage, essential tremor) or research studies to ensure accuracy, but it is not necessary in routine practice. This may change when there is a disease-modifying therapy, and making a correct diagnosis as early as possible is essential. Many efforts are underway to accurately define a premotor stage of PD with high sensitivity and specificity. There is also some evidence that the diagnosis of PD, and even pre-PD, may be made based on increased iron in the SN using transcranial sonography or particular MRI protocols.

3. Taxonomy. This section included the description of various datasets of brain MRI images, various data preprocessing techniques that can be applied to this dataset, and various DL models that can be used. The Fig. 3.1 shows the various subsection of taxonomy with their citations number. The detailed explanation is as follows.

3.1. Datasets. Pahuja *et al.* [42] used the Parkinson's Progression Marker Initiative (PPMI) dataset for detecting PD. This dataset provides brain MRI images of patients who have PD. Identifying the biomarkers of
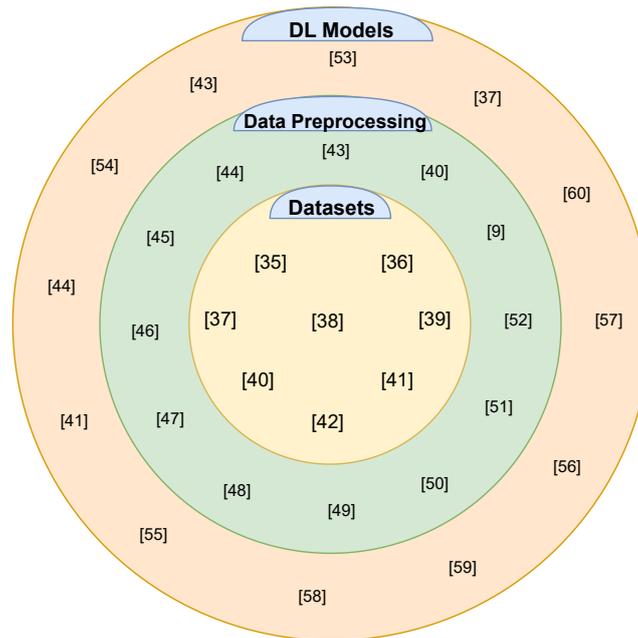
Fig. 3.1: Taxonomy chart

the Parkinson Progression is the primary goal of this dataset. They considered a 1.5T baseline 3D volumetric T1-weighted 150 brain MRI images. Half are healthy patients, and the remaining are PD patients. From the dataset, 72 images were replaced with 60 new illustrations due to error in the segmentation method.

Liu *et al.* [34] used the brain MRI dataset to diagnose PD. This dataset was accepted by Ethics committee, which was earlier associated with the Hospital of Jinzhou Medical University and then after the written consent was relinquish. This dataset contains the T2-weighted MRI images of patients, which were captured on a 3.0T MRI machine. They also used axial T1 weighted, axial Fluid Attenuated Inversion Recovery (FLAIR) and sagittal T1 weighted for anatomical references for Regions of interest (ROI) delineation and placement. Around 138 patients' MRI images, out of which 69 were healthy and 69 were PD-classified, were used as input for the model.

Yasaka *et al.* [67] enrolled patients with PD and HC who paid a visit to Juntendo University Hospital between February 2017 and October 2018 with the help of specialised neurologists who made the criteria for PD and examined them with a 3-T MRI unit using a 64-channel head coil. Multi-shell dMRI, Magnetization transfer saturation images and as result of which we got T1-weighted images for 115 PD and 115 healthy patients.

Wang *et al.* [64] used Quantitative susceptibility mapping (QSM) and T1-weighted MRI in their investigation to detect PD. They recruited 92 PD patients and 287 healthy people from Ruijin Hospital through QSM. The First Affiliated Hospital of Zhengzhou University obtained 83 PD and 72 healthy control data from T1-weighted MRI. The results from QSM were obtained utilising a 3T scanner equipped with a array head coil having 15 phased channel and a 3D Gradient echo sequences (GRE) imaging sequence. The data was gathered utilising a 3T scanner with a 64-channel phased array head coil and a 3D GRE imaging sequence from T1-weighted MRI.

Talai *et al.* [55] evaluated 45 PD patients, 20 with progressive supranuclear palsy, and 38 healthy individuals from the University Medical Centre Hamburg-Eppendorf's movement disorder outpatient clinic. Between July 2009 and September 2010, patient data were used for this investigation. They acquired DTI, T1-weighted Magnetization-Prepared Rapid Acquisition Gradient Echo MRI (MPRAGE), and triple-echo T2-weighted MRI datasets of each patient using a 3T Siemens Skyra MR scanner.

Table 3.1: Early detection PD metadata

Author	Year	Dataset Taken	Type of scan	Number of Subjects
Pahuja *et al.* [42]	2016	PPMI	T1-weighted MRI	75 PD, 75 HC
Liu *et al.* [34]	2020	Hospital data	T2-weighted MRI	69 PD, 69 HC
Yasaka *et al.* [67]	2021	Hospital data	T1-weighted MRI, dMRI, MT saturation images	115 PD, 115 HC
Wang *et al.* [64]	2023	Hospital data	T1-weighted MRI, QSM	92 PD, 287 HC & 83 PD, 72 HC
Talai *et al.* [55]	2021	Medical Center	T1-weighted MRI, T2-weighted MRI, DTI	45 PD, 20 Progressive supranuclear palsy, 38 HC
Pahuja *et al.* [43]	2022	Heterogeneous	T1-weighted MRI	73 PD, 59 HC
Shinde *et al.* [52]	2019	Medical Center	Neuromelanin sensitive MRI	45 PD, 20 Atypical Parkinsonian Syndromes, 35 HC
Ramírez *et al.* [46]	2020	Open Access Database	DTI	129 PD, 57 HC

Pahuja *et al.* [43] used the heterogeneous dataset of about 73 PD patients and 59 healthy individuals, which includes MRI scans, cerebrospinal fluid (CSF) biomarkers, demographic information. It includes neuroimaging data that 3D T1-weighted MRI scans and SPECT images (used to extract the specific binding ratio), whereas biological markers data includes four CSF markers.

Shinde *et al.* [52] used MRI, specifically Neuromelanin sensitive MRI dataset using a 3T MRI scanner, that contains the result of 55 subjects, includes 30 patients having PD and 25 HC, which was arbitrarily distributed into training and holdout sets, 25 HC and 30 PD patients for training and cross-validating the models remaining 10 HC and 15 PD patients for testing models.

Ramírez *et al.* [46] used the PPMI dataset, used T1-weighted images to extract subcortical Volumes of Interests (VOIs) using the free surfer software package of 129 PD patients and 57 healthy patients, that includes eddy current correction, brain extraction and tensor fitting. The authors used the DTI model to compare Fractional Anisotrophy (FA) maps, which were used as inputs in DL models.

The Table 3.1 shows the overview of datasets available for PD detection.

3.2. Data Preprocessing. Bhan *et al.* [8] used the MRIcro tool for data preprocessing on T1-weighted MRI images from the PPMI dataset to detect PD. Here, the image data were labelled between Parkinson's and healthy patients for feeding to the DL model based on respective T1w scans. Then, they sliced the lower part of each image as they did not contain any significant information, leaving with 10548 total images. Further, they used the TensorFlow library to read images. Based on this, they labelled the images of PD patients as 0 and healthy patients as 1, then split the data into training(90%) and testing(10%). Lastly, they applied One Hot Encoding and converted these integer values into binary values.

Sangeetha *et al.* [51] used a median filtering approach for data preprocessing on the PPMI dataset for diagnosing PD. This non-linear approach effectively reduces the noise of the MRI image and helps in preserving the edges of the MRI image. In this technique, firstly, each pixel is arranged in numerical order, and then every pixel of the image is replaced by the middle of its adjacent pixels. This filtering technique is so efficient that it can filter out minimal noise.

Zhang *et al.* [69] applied two data preprocessing techniques on their PPMI datasets to detect PD. Firstly, due to less availability of data samples, which may lead to underfitting or overfitting in DL models, they applied data generation by using Wasserstein generative adversarial network (WGAN) technology, and when the training epochs reached to the specific limit, after some interval, a new image MRI is generated and added to the original dataset. Secondly, to achieve diversity in the dataset to get a more accurate answer, they used the ImageDataGenerator API of the Keras model. They applied some basic rotations and inversion to the images at the end.

Bhan *et al.* [7] used image enhancement techniques on the PPMI dataset for diagnosing PD. This technique

Table 3.2: Data cleaning and transformation for early PD detection

Author	Year	Output	Process
Bhan *et al.* [8]	2021	Binary	MRIcro tool One Hot Encoding
Sangeetha *et al.* [51]	2023	Image	Median Filtering
Zhang *et al.* [69]	2019	Image	WGAN Technology ImageDataGenerator API
Bhan *et al.* [7]	2021	Image	CLAHE Gaussian blur Histogram Equilizer
Camacho *et al.* [12]	2023	Image	HDBET ANTs log-Jacobian maps
Rubbert *et al.* [48]	2019	Image	FMRIB BET2 FIX
Pereira *et al.* [44]	2023	Image	Visual Rhythm approaches
Noor *et al.* [40]	2020	Image	Motion correction Spatial normalization Scaling Feature extraction
Veetil *et al.* [62]	2023	Image	Skull stripping Bias field correction Normalization Data augmentation
Erdaş *et al.* [23]	2023	Image	Image registration using python code
Chakraborty *et al.* [13]	2020	Image	Image registration

removed unwanted noise, colour, brightness, etc. This was done by applying image filtering techniques and using a histogram equaliser to increase the contrast and quality of images. For enhancing the image, the RGB(red, green and blue) images were converted to the most commonly used colour encoding scheme, that is, luma (brightness (Y), blue projection (U) and red projection (V))(YUV) channels. After the conversion, they used the Gaussian blur function to filter extra noise and pixels. To improve contrast in images the Contrast-limited adaptive histogram equalization (CLAHE) technique was used. Finally, the luma (brightness (Y), blue projection (U) and red projection (V))(YUV) channels were combined and converted into red, green and blue(RGB) colour space.

Camacho *et al.* [12] used the following steps to process T1-weighted pictures. HD-BET was used to eliminate all non-brain tissues from original MR images for brain extraction. The resulting images were then aggregated using linear interpolation to an isotropic resolution of 1 mm. The bias field was corrected in the second step using the non-parametric non-uniform intensity normalisation technique from the Advanced Normalisation Tools (ANTs) toolkit version 2.3.1. The T1-weighted MRI data were then non-linearly registered to the MNI PD25-T1-Magnetization-Prepared Rapid Acquisition Gradient Echo MRI (MPRAGE) 1 mm brain atlas (fixed image). After aligning the data to the atlas transformation, they employed ANTs to initialise the non-linear registration in the second step.

Rubbert *et al.* [48] used whole brain resting state resting state fMRI (rs-fMRI) to discriminate PD patients from healthy patients. To pre-process the rs-fMRI data, they took the help of the Oxford Centre for FMRIB Software Library(FSL) version 5.0. Brain extraction was performed by Brain Extraction Tool of fMRI of the

Brain (FMRIB) . After smoothing the image with a Gaussian kernel and normalisation, They used FMRIB's ICA Xnoisifier to automatically denoise rs-fMRI data.

Chakraborty *et al.* [13] acquired their research data from the PPMI dataset. So, to solve the differences, as the data has been collected from multiple centres worldwide, the images needed to be in the same space as their references, so they performed an image registration procedure. The image registration procedure was performed on the source images(in this study, the PPMI dataset), and the atlas, such as MNI and Individual Brain Atlases using Statistical Parametric Mapping (IBASPM), were identified as target images. They executed the registration of the MRI scan using symmetric normalisation using a tool known as Advanced Normalization Tools Python (ANTsPy).

Erdaş *et al.* [23] also used the image registration procedure to integrate the PPMI dataset to convert unseen or unknown images into adequately aligned fixed images. With the source image as PPMI and target image as Montreal Neurological Institute(MNI), the procedure was executed with 152 T1-weighted linear 1 millimetre (mm) atlas by making completely automated code in python based upon FLIRT registration tool linked with the FMRIB Software Library(FSL) using BET method to remove unnecessary tissues, bones, skin, fat and other bodily structures to increase the performance of the method to be applied on the given MRI dataset.

Pereira *et al.* [44] used an intelligent pen to extract information from handwritten dynamics and applied a normalisation step to input signals. In this, they used a filter bank to remove features such as edges and corners, and they then developed a CNN to learn pen-based features; they also mentioned that the CNN is composed of several layers, each of which is responsible for learning a different and finer representation of the data and textures from an image from input signals: helps to improve the performance of DL algorithms by ensuring that the input data is on a similar scale.

Veetil *et al.* [62] used several Data pre-processing techniques to prepare the MRI data for analysis. These techniques include skull stripping, bias field correction, and normalisation. Skull stripping eliminates non-brain tissue from the MRI images, while bias field correction is used to correct intensity inhomogeneities in the images. Normalisation is used to standardise the intensity values of the images. Moreover, the authors used Data augmentation techniques like rotation, flipping and scaling to increase the dataset's size and improve the models' robustness. The experiment progessed by taking an 80-20 training-testing, spliting augmented images. Then normalising the image intensities to the range of 0 to 1 for gaining monotonicity in the intensity and thus helps in contrasting across all images.

Noor *et al.* [40] used techniques that included motion correction, Spatial normalisation, and scaling. They also mentioned the importance of feature selection and extraction in achieving accurate results and summarised the features used in each study. Overall, the paper enlighten the importance of data preprocessing in careful way and selection of feature in achieving accuracy and reliability in DL applications for PD.

Pahuja *et al.* [43] used three primary image data preprocessing techniques before applying VBM, mainly Spatial normalisation (SPM8), Unified Segmentation (SPM8), used to segment images into various tissue types such as grey matter, cerebrospinal fluid that allow for identification of differences in tissues between individual, Smoothing used to reduce noise in images and additionally for feature extraction smoothed modulated GM volumes are used.

The Table 3.2 shows overview of various data preprocessing approaches that can be applied.

3.3. DL Models. Kumaran *et al.* [32] used modified Visual Geometry Group (VGG) Net Architecture, the standard CNN, to detect PD. They compared four different architectures and found the modified VGG Net architecture to be the best in accuracy. This architecture contains many blocks, and each block has a 2D convolution. They took the swallow tail sign from the brain MRI as an input variable to that model. The VGG Net model can detect around 1000 object categories like keyboard, person, mouse, animals, birds, pencils, etc. Through this model, they achieved approximately 93% of efficiency in detecting PD.

Bhan *et al.* [8] used LeNet-5 architecture for the early detection of PD. LeNet-5 architecture is a type of CNN. This model includes two Conv2D, two pool layers and a hidden layer. Their baseline model has 2 dense layers. The first layer includes of ReLu activation along with 128 neurons, and the second layer includes of a Sigmoid activation function followed by two neurons at each thick layer. They used a batch size of 32, and the number of epochs was 30. This model gave approximately 96.6% accuracy on training dataset and 97.6% accuracy on testing dataset with a loss of 0.07 percentage with no batch normalisation. When the same model

Table 3.3: Performance stats of DL model for early detection of PD

Author	Year	Objective	Pros	Cons
Kumaran et al. [32]	2022	Early and accurate detection of PD from brain MRI scans	Accomplished 93% accuracy in PD detection	Cannot detect the stages of PD
Bhan et al. [8]	2021	To increase the chance of curing through early detection	Attained 97.63% accuracy in PD detection	Can't analize medical or neuro images
Sangeetha et al. [51]	2023	To precisely diagonise PD using CNN model	Acheived 95% accuracy in PD detection	Medical picture analysis are less efficient
Kollia et al. [31]	2019	To enhance PD detection using CNN-RNN model on MRI	Reached 98% accuracy in PD detection	Absence of diagnosing neurodegenerative disease
Shinde et al. [52]	2019	Create diagnostic biomarkers of PD using NeuroMelanin-sensitive (NMS-MRI)	Obtained 80% testing accuracy compared to Radiomics based classifier (RA-ML) with its accuracy being 60%	Dependent on the testing ability of the method to differentiate between PD and other parkinsonian disorders
Sivaranjini et al. [53]	2019	Diagnosis of PD using CNN	An accuracy of 88.9% is achieved through proposed method	Low Performance level beacause of less tuned AlexNet model
Kaplan et al. [27]	2022	Early Diagnose of PD	An Accuracy of 99.53, 99.22,98.70 % is obtained from various datasets	the accuracy of the classification may be limited by the number and quality of features used
Choi et al. [16]	2017	Diagnosis of PD via DAT imaging interpretition	Improved performance in image classification:DAT(98%)	Carefull analysis and evaluation of performance and limitation are required
Yasaka et al. [67]	2021	Investigate the use of DL techniques to differentiate PD patient from Healthy patients	Accuracy: 67%-89%, AUC of 0.895,0.800,0.761 for (RK-weighted matrix, AK-weighted, ICVF&AVF-weighted matrices)	relative small sample size, lack of eternal validation, single-centre dataset, lack of generalizability of CNN
Khairnar et al. [29]	2023	Development of deep-learning method for early prediction of PD	Proposed the more reliable method for PD detection using CNN	Haven't used CNN & Artificial Neural Networks (ANN) model to give cost effective prediction of PD
Sahu et al. [50]	2021	Efficient detection of PD using DL technique	Obtained 93.46% of accuracy comparing other existing approaches	Less DL tools are used

is used with batch normalisation, the accuracy of training dataset is 95.4%, and the accuracy of testing dataset is 97.9% with a loss of 0.05%.

Kollia et al. [31] used Deep Neural Network (DNN) based CNN and CNN-RNN for diagnosing PD. The Residual Network-50 (ResNet) structure was used for the pooling and convolutional part. The Gated Recurrent Units (GRU) was utilised in the RNN part of the CNN-RNN architecture. Firstly, the CNN-RNN model was trained with training MRI datasets. It gave around 70.6% performance on the testing dataset, then after the performance was enhanced by changing the value of the modified Loss Function. The CNN model with two completely connected layers and no hidden layer gave around 94% accuracy. The CNN-RNN architecture with a single fully connected layer and two hidden layers gave around 98% accuracy.

Sangeetha *et al.* [51] applied CNN on brain MRI images for PD detection. The main reason for applying this model was the spatial nature of the model, because of which the number of hyper-parameters was reduced. They used five convolutional levels with ReLu activation at each layer; at the first level, there were 16 filters. At the second level, there were 32 filters, and the third, fourth and fifth layers contained 64 filters. Their model includes five max pooling layers and a flattened layer in the middle of the first dense layer and last pooling layer. Moreover, there was ReLu stimulation in all 128 primary levels and SoftMax activation in 2 layers, making 130 dense layers. The model reached to 95% accuracy with specificity and sensitivity of approximately 97%.

Shinde *et al.* [52] advised a computer-based analysis algorithm that uses a CNN to produce (NeuroMelanin-sensitive(NMS)) NMS-MRI diagnostic biomarkers for PD. They employed a standard CNN architecture acquired from ResNet design, which is considered good in image classification related to the medical field. They also compared Contrast Ratio Classifier (CR-ML) and Regression Analysis (RA) with their proposed method. They obtained higher accuracy, sensitivity and specificity compared to radiomics with their novel approach, with the accuracy of RA being 81.8% and CNN-DL's accuracy being 83.6% in cross-validation.

Chowdhary *et al.* [18] used a computer vision method to make the process of detection of PD more refined. They used histogram of oriented gradients (HoG) as a feature extraction method and used CNN, which is based on sequential model, for a lightweight model. Using this proposed model they achieved 94% accuracy with specificity and sensitivity as 92% and 80%. The proposed model can be used on embedded and hand-held devices for a quick self-analysis.

Sivaranjini *et al.* [53] analysed T2-weighted MR images of the brain for detecting the PD using CNN pre-trained model named AlexNet. AlexNet, which comprises many layers like the input layer, convolution layer, pooling, dropout layer and fully connected layer, helps to classify the input data images in PD and healthy patients using mandatory operations. The presented method's performance of pre-trained AlexNet CNN model is determined by measuring its accuracy, specificity and sensitivity. They obtained these parameters of their proposed approach and compared them with other methods. They achieved 88.9% accuracy, 89.3% sensitivity and 88.4% specificity with their approach.

Khairnar *et al.* [29] presented a CNN and ANN based method using MRI and SPECT scans. They applied data pre-processing techniques on the MRI dataset like image resizing, augmentation, normalisation and noise removal. And then pre-processed data were then given to already trained CNN model. While applying the pre-processing techniques like on the MRI scans with the difference of data cleaning instead of image resizing and feature selection instead of noise removal on the SPECT dataset, they trained the ANN model on the SPECT dataset.

Sahu *et al.* [50] used a mixture of RA and ANN to detect the disease by probability estimation using these DL tools. They also estimated the predefined edge of the neurons to the patients' vocal recognition, content of iron, and pulse rate data. RA is used to pre-process the data, and then the pre-processed data is fed to the trained ANN model. The calculated probability values and the five attributes obtained by RA are stored in a file and then used to produce the probability of PD with ANN. After evaluating the final output, they compared it with other approaches and found their accuracy of 93.46% with a specificity of 67.34% and sensitivity of 95.64% of their proposed approach. They executed their proposed algorithm's stimulation with the help of C language with the Scientific Laboratory (SCILAB) program for graph plotting.

Kaplan *et al.* [27] employed two classifiers and a combination of feature extraction and classification techniques to achieve accuracy. The k-nearest neighbour (kNN) algorithm produces the best results for clinical staging and PD motor symptom classification, and k is a hyperparameter that may be adjusted to improve classification accuracy. Whereas Support Vector Machine (SVM), a type of supervised learning algorithm that finds the optimal hyperplane that distinguishes data points of different classes with the most significant margin, is effective for high-dimensional data and can handle noisy data, it is sensitive to the kernel function and hyperparameters used. As a result, the classifier produced the best classification results for dementia status categorization.

Choi *et al.* [16] used a DL-based system, a type of ANN particularly well suited for image classification tasks. Mainly, a CNN was used to train the system on SPECT images of PD patients and healthy patients. Once the CNN is trained, it can accurately classify SPECT images as PD or non-PD. Compared to the traditional methods followed by humans for the interpretation of FP-CIT-SPECT imaging, the DL-based model system
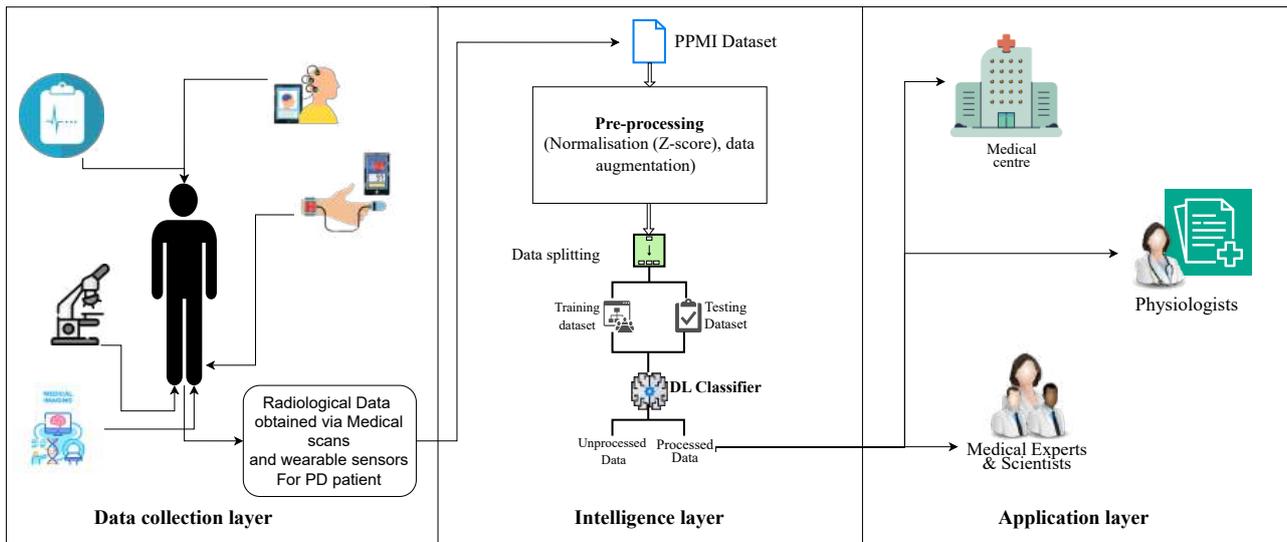
Fig. 4.1: Case study overview

can overcome the variability of human evaluation and provide more objective patient group classification. A particular audience for the same are patients with uncertain Parkinsonism and for the classification of atypical subgroups, for example, SWEDD.

Shivangi *et al.* [26] used the first model, VGER Spectrogram Detector, which takes spectrogram images as input and then used a CNN to categorize the data into one of three classes: healthy,early-stage PD. The next one or second model is the Voice Impairment Classifier, as input we using elabrated features of speech images and uses a stacked autocoder (sAE) to classify the images into severe or not severe PD. They were trained and tested for the balanced datasets that contained almost equal proportions of all the classes.

Yasaka *et al.* [67] used a DL method called CNN for the classification of PD patients and healthy patients. Input data was parameter weighted, and the structural connectome matrices vary according to the number of streamlines was thus evaluated from dMRI and was trained with high accuracy. They also used gradient-weighted class activation mapping (Grad-CAM) to visualise the regions of the connectome matrices, which were essential during CNN's decision making process. The Table 3.3 shows the brief of various DL models for early detection of PD.

4. Case study.

4.1. Data collection layer. We gathered a PPMI dataset by setting specific options; for the machine, we chose the Seimen machine, and the images were grey. This dataset included 970 PD patients and 210 healthy individuals. These individuals underwent 3D MRI scans as part of the study. We used preprocessed MRI images that were converted into 3D Numpy arrays. Numpy arrays are a well-known and feasible data structure for numerical operations in Python, which makes it suitable for feeding the data into DL models. Fig. 4.1 demonstrates the overview of case study we performed.

4.2. Intelligence layer. Data is being processed and prepared for training and testing purposes for the CNN model.

4.2.1. Data Preprocessing. In our study, we used Z-Score Normalisation, which was then applied to the MRI data so that the pixel has a mean of zero and ensures a standard deviation of one. This aids in lowering data variance and qualifies it for machine learning model training.

4.2.2. CNN model. We chose CNN model for the analysis. CNNs are particularly well-suited for image data because they can automatically learn features from the images. The preprocessed 3D Numpy arrays served
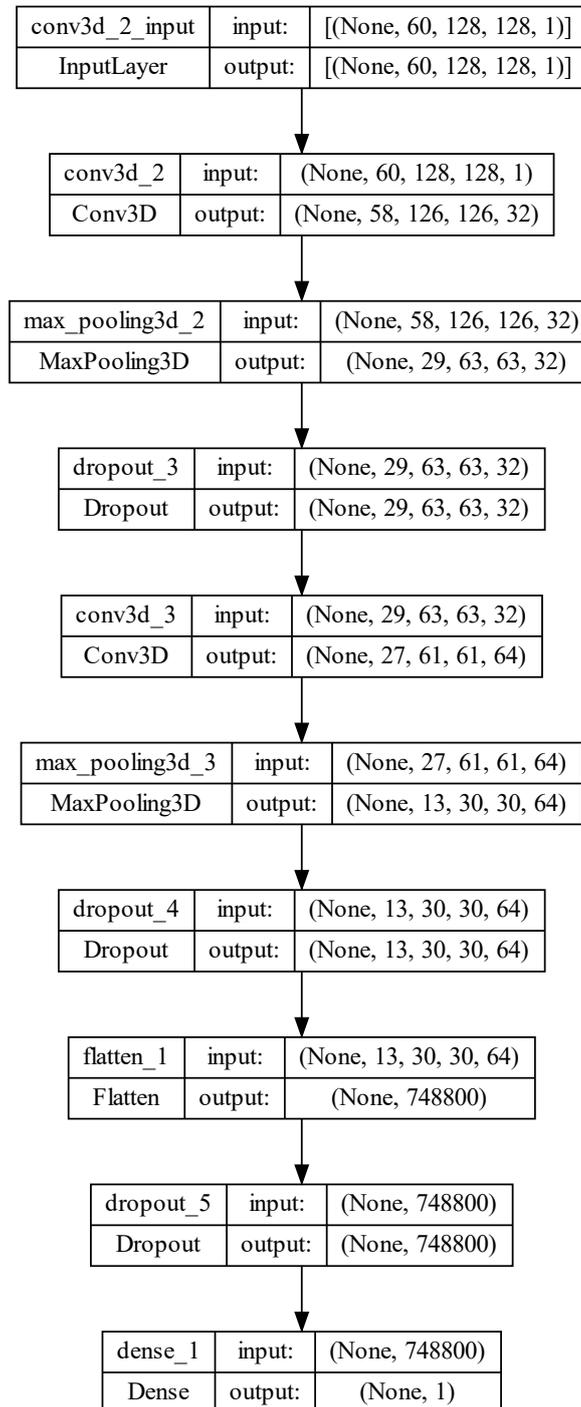
| conv3d_2_input | input: | [(None, 60, 128, 128, 1)] |
| InputLayer | output: | [(None, 60, 128, 128, 1)] |

| conv3d_2 | input: | (None, 60, 128, 128, 1) |
| Conv3D | output: | (None, 58, 126, 126, 32) |

| max_pooling3d_2 | input: | (None, 58, 126, 126, 32) |
| MaxPooling3D | output: | (None, 29, 63, 63, 32) |

| dropout_3 | input: | (None, 29, 63, 63, 32) |
| Dropout | output: | (None, 29, 63, 63, 32) |

| conv3d_3 | input: | (None, 29, 63, 63, 32) |
| Conv3D | output: | (None, 27, 61, 61, 64) |

| max_pooling3d_3 | input: | (None, 27, 61, 61, 64) |
| MaxPooling3D | output: | (None, 13, 30, 30, 64) |

| dropout_4 | input: | (None, 13, 30, 30, 64) |
| Dropout | output: | (None, 13, 30, 30, 64) |

| flatten_1 | input: | (None, 13, 30, 30, 64) |
| Flatten | output: | (None, 748800) |

| dropout_5 | input: | (None, 748800) |
| Dropout | output: | (None, 748800) |

| dense_1 | input: | (None, 748800) |
| Dense | output: | (None, 1) |

Fig. 4.2: CNN_Layered_Architecture

as input to the CNN, and we used data augmentation to generate more samples of healthy patients artificially. Standard data augmentation techniques for images include rotation, flipping, cropping, and changing brightness or contrast. The researchers created variations of the original MRI images by applying these transformations, effectively by expanding the dataset. The detailed architecture is being shown in the Fig. 4.2 The input grey scale MRI images had 60 layers in which each layer of size 128×128, whereas "None" in the input shape (None, 60, 128, 128, 1) means that the network can accept variable batch sizes for input data while keeping the other dimensions fixed. The number of PD patient images was 970, and the number of healthy patient's images was 210 before and 840 after augmentation. There were a total of 100 epochs with the batch size of 32. So, the total trainable parameters were 1553861. The CNN model was initially trained on the preprocessed data without data augmentation, which resulted in a 65% accuracy rate in distinguishing between PD and healthy subjects, as shown in the figure. This accuracy level indicates the model's performance before data augmentation. After data augmentation, the model's accuracy remarkably improved to 88%, as shown in the figure. This depicts that data augmentation substantially enhanced the model's capability for distinguishing between PD and healthy patients.
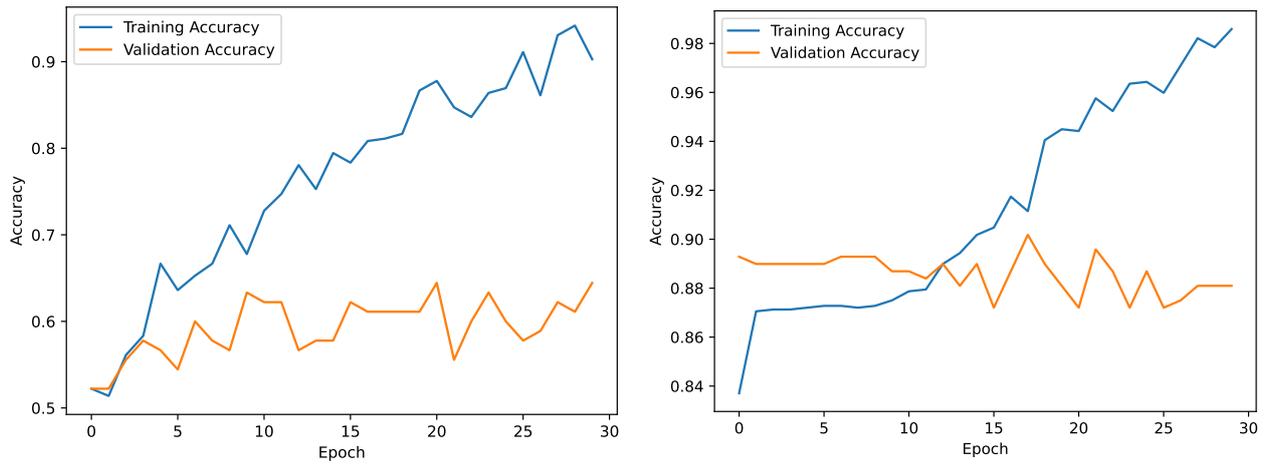
4.3. Application layer. If the result demonstrates high accuracy and reliability, it can be integrated into clinical workflow. Surgeons and healthcare experts can access the result/model through a user-friendly interface or software application. These results give surgeons a broad perspective for deciding the supporting tool or aid in diagnosing or treating PD. By analysing patient data, genetic information and biomarker data (that are critical for tracking disease progression) that is used for evaluating the effectiveness of potential vaccines and treatments, this information can guide researchers or scientists in developing vaccines that target species, aspects of the disease such as abnormal proteins aggregation or neuro-inflammation. Also, the insights gained from the results are helpful for the development of drugs or therapies that might alleviate symptoms or slow down disease progression. These results too provide valuable information for tailoring vaccine or treatment strategies to individual patients based on their specific disease profiles since results are divided into subgroups of patients with varying disease characteristics. Researchers and vaccine developers can use the results of machine learning models to review existing literature, clinical studies, and relevant datasets more efficiently, potentially uncovering previously overlooked insights or connections.

5. Performance Analysis of presented case study. We have used MobaXterm supercomputer as our virtual environment for coding in Python. The supercomputer has installed Ubuntu 20.04.6 LTS as its operating system and has RAM of 250 Gigabytes and Virtual RAM of 32 Gigabytes. With these computer parameters, we began fitting MR scans of PD and HC patients to our model and achieved the following results. Fig. 5.1b shows the accuracy of our model on the scans of PD and HC patients; after we applied data augmentation as a pre-processing technique, it suddenly increased by about 20 %, as shown in Fig. 5.1a. The model was trained through trial and error method, So it took around 1 week to completely train the model.

Fig. 5.2a demonstrates the function of loss in training of data on the chosen model without applying data augmentation, but after referring to Fig. 5.2b, it becomes apparent that the decreasing loss in the validation process is due to data augmentation.
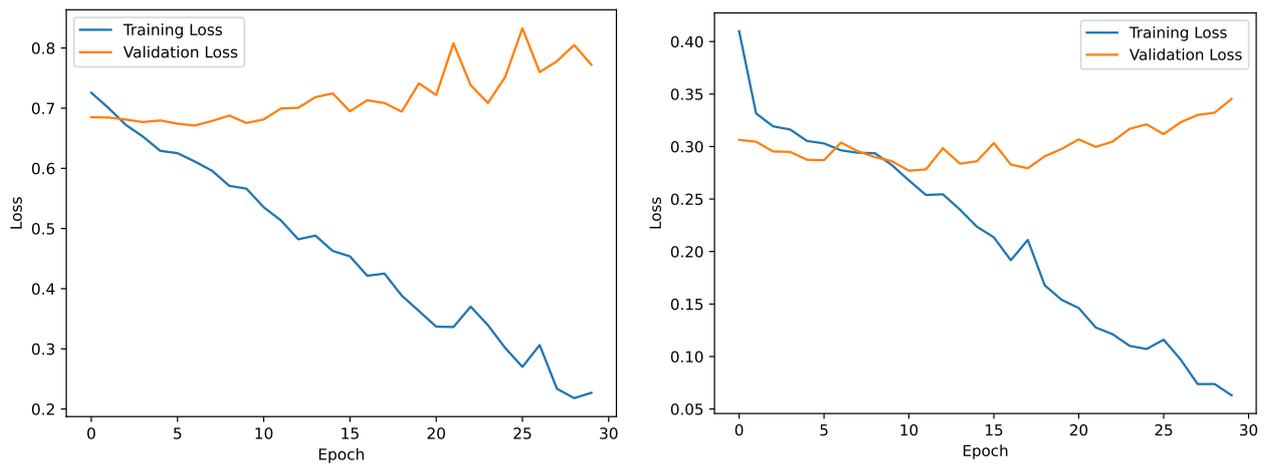
Fig. 5.3b represents a confusion matrix for our model, which shows the numerical data of medical scan identifications for true PD and true Healthy patients after applying data augmentation. These results are significantly higher than the results obtained before using data augmentation as a pre-processing technique, as shown in Fig. 5.3a.

6. Research Challenges. Early detection for PD using DL on MRI datasets is an active area to go for research. However, it does come with some difficulties. Limited availabilities of high-quality datasets on 3D-MR images can make whole research work in vain [1]. The quality and quantity depends on various sources and scanning factors, which is the ultimate reason for biasing. One major bottleneck is feature selection that is identifying the features from MRI data that helps distinguish early-stage PD patients from healthy patients. Also, the models like CNN are known as "Black Boxes" analysing the results and their decisions are quite challenging [47]. Moreover, hardware inconsistencies may affects the performance and accuracy results of DL that is considerable point that makes it more challenging to go for [60]. Collecting the longitudinal data that is important for early diagnosis that is used to track PD progression, which is a cumbersome task [21]. Also,

(a) Training and validation accuracy graph before data augmentation

(b) Training and validation accuracy graph after data augmentation
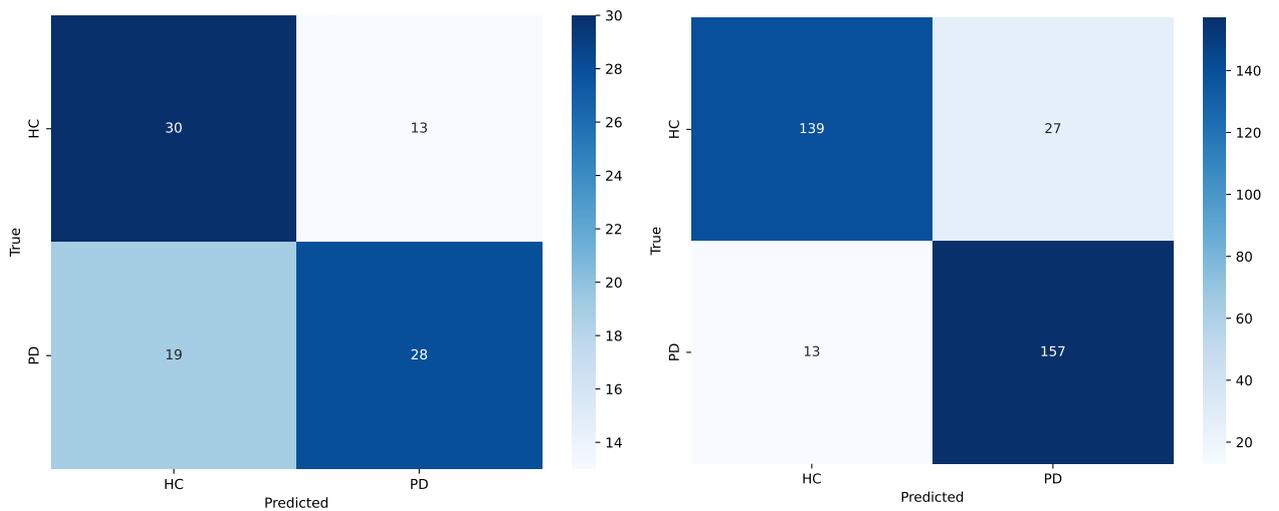
Fig. 5.1: Accuracy Graphs of Model training

(a) Training and validation loss graph before data augmentation

(b) Training and validation loss graph after data augmentation

Fig. 5.2: Loss graph of model training

to gather diverse MRI datasets and then segmenting them and applying model architectures in order to ensure the quality, performance and accuracy of results would require collaborations between doctors, clinical experts, data scientists and researchers, which is a crucial and more challenging task [38].

Biomarkers and AI will be critical in the future of PD diagnosis. While genetics remains important, the majority of cases include complicated genetic factors interacting with environmental circumstances. This understanding might open the way for the application of AI to predict disease progression and features. Radio-logical imaging studies and genetic markers may play important roles in early diagnosis, making PD a biomarker-supported disorder. Nonetheless, a rising number of medications for disease modification are being devel-

(a) Confusion matrix for CNN model before data augmentation

(b) Confusion matrix for CNN model after data augmentation

Fig. 5.3: Confusion matrix of model training

oped, but obstacles remain, particularly for asymptomatic patients who may not have access to preventive medicine [57].

7. Conclusion. In this paper, we conducted a detailed analysis of the disease covering ts causes, symptoms, and conventional treatment methods. We have also covered a broad range of various datasets, explored different data preprocessing techniques, and a wide range of DL models that was being practised by authors for early detection of PD. The approach of this paper is kept simple and straightforward, so that it can be easy to understand .In our case study, we used 3D brain MRI images of 840 healthy control and PD from the PPMI dataset on which we have applied various data preprocessing techniques and employed CNN for the model. Through this, we have achieved an eminent accuracy of 88%. Our study underscores the potential of advanced technologies to revolutionise early detection and remedial approaches, provides a hope to those who are struggling with the ailment.

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