Model for MRI-Based Detection and classification of Parkinsonian Tremor and PIGD

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Final Thesis Report

Abstract

Parkinson's disease (PD) is a long-term, developing neurodegenerative condition that severely impacts both movement and non-movement activity, impacting millions of individuals worldwide. Early diagnosis of PD is crucial for initiating timely interventions which can slow disease progression and enhance patients' quality of life. However, current diagnostic techniques are based on clinical symptoms that manifest only after considerable neuronal damage has occurred, often leading to delayed diagnosis. This research proposal seeks to develop a novel and reliable method for the preliminary identification of disease using deep learning methods.

The recommended study will focus on analyzing medical imaging data, particularly magnetic resonance imaging (MRI), along with other clinical biomarkers, to identify early indicators of PD and classify into tremor and PIGD before the onset of noticeable symptoms. By employing state-of-the-art deep learning technique, the research seeks to develop a predictive model that can accurately differentiate between Parkinson's disease patient and healthy individuals.

The research will utilize a comprehensive dataset comprising MRI scans and clinical data from tremor PD patients, PIGD PD patients and healthy individuals. Deep learning model will be trained and validated on this dataset to ensure robustness and accuracy. The study's outcome is expected to contribute significantly to the field of neurodegenerative disease research by providing a tool that could facilitate earlier diagnosis, potentially leading to better patient management and treatment outcomes.

The findings from this research could pave the way for the integration of AI-driven diagnostic tools in clinical practice, offering a non-invasive, efficient, and scalable solution for the identification and classification of Parkinson's disease.

Table of Contents

Contents

Abstr	act	2
CHAI	PTER 1	
INTR	ODUCTION	
1.1	Background	
1.2.	Related Research	
1.3	Aim and Objectives	
1.4	Scope of the Study	
1.5	Significance of the Study	
1.6	Structure of the Study	
CHAI	PTER 2	
LITE	RATURE REVIEW	14
	PTER 3	
METI	HODOLOGY	18
3.1	Introduction	18
3.2	Dataset Acquisition	19
3.3	Image Preprocessing	19
3.4	Image data generator and segmentation	20
3.5	Model Evaluation	20
3.6	Feature Extractor and model classification	2
3.7	Summary	22
Chapt	er 4	
ANA	LYSIS AND DESIGN	22
4.1	Introduction	22
4.2	Dataset Preparation	23

4.3	Data Augmentation	24
4.4	Training Data Setup and Hyperparameter tuning.	25
4.4.1	Conventional CNN	25
4.4.2	Dense Net Model	27
4.4.3	ResNet Model	28
4.5	Summary	30
	PTER 5	
RESU	JLT AND DISCUSSION	31
5.1	Introduction	31
5.2	Validation Dataset Test Result	31
5.3	Validation data Result Discussion	34
5.4	Summary	34
CHAI	PTER 6	35
CON	CLUSION AND RECOMENDATION	35
Refere	ences	36
	LIST OF TABLES	
	1: Related Research of behavioural Patten	
Table	2 Related Research of behavioural Patten	10
Table	3 Symptoms of Parkinsons	14
Table	4 Gender of Patient	19
Table	5 Types of Patients	19
Table	6 Evaluation Matrix	20
Table	7 Disease Detection metrics	31
Table	8 Disease classification metrics	31
Table	9 CNN model Vs pretrained model	31

LIST OF FIGURES

Figure 1 Methodology Flow Chart	18
Figure 2 CNN Model Architecture	
Figure 3 Classification of Disease Dataset	23
Figure 4 Detection of Disease Dataset	
Figure 5 Sample Image	24
Figure 6 Augmented Image	25
Figure 7 CNN Architecture	20
Figure 8 Accuracy Epoch chart	20
Figure 9 Dense Net MRI image	27
Figure 10 Dense Net model accuracy graph	28
Figure 11 Resnet MRI image.	
Figure 12 ResNet model Accuracy graph.	
Figure 13 Confusion Matrix of disease detection	
Figure 14 Confusion Matric of disease classification	33

LIST OF ABBREVIATION

MRI	Magnetic Resonance Imaging
PD	Parkinson's Disease
PIGD	Postural instability and Gait disorder
TD	Tremor Dominant
AI	Artificial Intelligence
CNN	Convolution neural network
VGG	Visual Geometry Group
LSTM	Long short-term memory
2D	Two Dimensional
PPMI	Parkinson's Progression Markers Initiative
UCI	University of california helath
MDVP	Multi-Dimensional Voice Program
PWP	People with parkinson Disease
ML	Machine Learning
SVM	support vector machine
ROC	Receiver Operating Characteristic

AUC Area under ROC curve
REM Rapid eye movement
CAD Computer-aided design
ASL Arterial spin labeling
DAT Dopamine Transporter

NTUA National Technical university of athens

DNN Deep neural Network
RNN Recurrent neural network
PET Positron emission tomography

SPECT Single photon-emission computed tomography

DTI Diffusion Tensor Imaging
T1 1 tissue type is bright – FAT

T2 2 tissue types are bright – FAT and WATER

HC Healty Cohort

GPU graphics processing unit SSD solid-state storage device

OpenCV2 Open Source Computer Vision Library

PwPD People with aprkinson disease
NSD neuronal alpha-synuclein disease
CSF alpha-synuclein in cerebrospinal fluid

GBA1 Glucosylceramidase Beta 1

SWedd Scans Without Evidence of Dopaminergic Deficit

ReLU Rectified Linear Unit ResNet Residual Network

DenseNet Densely Connected Convolutional Networks dcm Digital Imaging and Communications in Medicine

png Portable Network Graphic

GCase9 glucocerebrosidase

CHAPTER 1

INTRODUCTION

1.1 Background

Parkinson's disease (PD) is a core neural network dysfunction that often impacts movement, frequently causing tremors. It is characterized by the death of neurons in the midbrain that produce dopamine (Wroge et al., n.d.). Parkinson's disease (PD) is a developing Nervous system-degenerative condition that predominantly impacts movement function, characterized by signs such as tremors, bradykinesia, rigidity, and postural instability (Pir masoom et al., n.d.). It is the second most common neurodegenerative disease after Alzheimer, impacting millions of individuals worldwide, and its prevalence continues to rise with the aging population (Obeso, 2010). Symptoms of PD start with tremor in single hand, patient condition gets worse as time passes. Disease starts because of loss of dopamine in brain, dopamine is chemical release by neuron to send signal to another neuron (Pir masoom et al., n.d.). Hence timely detection of disease is very important. "It is believed that 25% of diagnoses are incorrect (Tolosa et al., 2006)". "The accurate detection of PD is still a challenging task (Pir masoom et al., n.d.)". Despite significant advancements in understanding the pathology of PD, early and accurate diagnosis remains a critical challenge. Current diagnostic methods rely heavily on clinical evaluation and the presence of motor symptoms, which typically appear only after substantial neuronal loss has occurred. There is no specific biomarker, blood test etc. to detect Parkinson's, due to this disease gets detected at advance stage and become uncontrollable.

Researchers have explored multiple options to detect and classify the disease at an early stage. They have used various modalities and images, like handwriting, speech behavior, voice signal, walking pattern. MRI images etc. to detect Parkinson's. They have tried to find a common pattern among healthy, tremor and PIGD patients and successfully developed model for the same. Existing research has its own limitations like limitation of datasets, researchers have not combined multiple modalities etc. It is mentioned in detail in related work sections. Hence, we need to do further research to develop a robust model which will help patients and doctors in early detection of patients.

This research proposal aims to explore and develop an innovative method for detection of Parkinson's disease at a preliminary stage with deep learning algorithms. By utilizing a combination of scan image modality such as MRI and other relevant clinical data, this research seeks to develop a robust predictive model that can accurately identify early markers of PD. The proposed research will not only contribute to the body of knowledge in the field of neurodegenerative diseases but also has the potential to revolutionize diagnostic practices, leading to better patient care and management.

We will use a large dataset with variation of MRI images to detect and classify the disease. CNN model is being used in this research as it is a proven technology with MRI image to detect various disease in past, (Billones & Olivia Jan Louville D. Demetria, 2016) optimized VGGNet for Alzheimer identification and obtained accuracy of 91.85%. (Dou et al., 2016) attained accuracy of 93.16% in detecting cerebral microbleeds in MRI scans. MRI images are preprocessed,

then split into train, test, and validation dataset and finally CNN models are implemented on training set and evaluated on testing dataset. We will evaluate the model with coefficient metric, accuracy, precision, recall, F1 score and then we will compare it with various existing state of art models.

The following sections of this proposal will outline the specific objectives of the study, the methodology to be employed, the expected outcomes, and the potential significance of the research. Through this comprehensive approach, we aim to address the pressing need for improved diagnostic tools in Parkinson's disease and contribute to the broader goal of enhancing patient outcomes in neurodegenerative diseases.

1.2. Related Research

Parkinson's disease (PD) is a progressive neurodegenerative disorder that is affecting millions of people in developed and developing countries. PD disease is more seen in aged people, and it affects the lifestyle of the patient. This disease cannot be cured completely but it can be controlled and improved by accurate and early detection. Diagnosis method which relies on clinical method is time consuming, subjective, and expensive. Diagnosing it at the starting phases of disease has proven to be challenging. Hence fast & accurate detection and classification of disease is required. Previous researchers have concentrated on enhancing the accuracy of disease detection.

Researcher has created a model to diagnosed disease though voice or speech analysis, walking pattern and handwriting pattern etc. in Table 1. Researcher has created model to detect disease using MRI images mentioned in Table 2

Table 1: Related Research of behavioural Patten

References	Year	Title	Author(s)	Dataset	Problem(s)	Purpose	Algorithms	Evaluation	Summary	Remarks
(Naanoue	2023	"Parkinson	Jana	Department	It is not	Purpose of	It uses Deep	Confusion	In this paper,	То
et al., 2023)		's disease	Naanoue1,	of	complete	the research	learning-based	matrix has	an LSTM	increase
		detection	Reem	Neurology	and	is to detect	model using	been	based deep.	accuracy,
		from	Ayoub1,	in the	accurate.	Parkinson's	long-short term	created and	learning model	exploring
		speech	Farouk El	Faculty of		disease from	memory	Precision,	is used to	the
		analysis	Sayyadi1,	Medicine,		speech	(LSTM)	recall, F1	detect	combinat
		using deep	Lara	Istanbul		analysis	model. It	score and	Parkinson's	ion of
		learning."	Hamawy1,	University			detects	accuracy	disease form	multimod
			Ali Hage-				Parkinson's		voice signals.	al
			Diab1, Fatima				disease using		The mode is	informati
			Sbeity1,2				speech dataset		trained using a	on could
							of Parkinson's		voice	be
							disease		recording	advantag
							patients and		dataset of	eous for
							healthy people.		Parkinson	diagnosin
									disease patient	g
									and healthy	Parkinso
									patient.	n's
										disease

(Pereira et al., 2016)	2016	"Deep Learning- Aided Parkinson's Disease Diagnosis from Handwritte n Dynamics"	Clayton R. Pereira Silke A. T. Weber Christian Hook Gustavo H. Rosa, Jo~ao Papa	Faculty of Medicine of Botucatu, S~ao Paulo State University, Brazil	Dataset is small and not accessed on patient in the initial stages of PD	Detection of Parkinson's using handwriting behavior	The CNN was trained through supervised learning on the dataset comprising samples from both healthy subjects and those with PD	Overall accuracy is computed using the standard formulation , i.e., (1 – errors/ dataset size) *100, which is around 84-87 %	In this paper, we model handwritten data as a time series and feed it into a CNN, which can learn features to differentiate between healthy individuals and PD patients.	Test should be done on dataset with more exams as well as with more individua ls. To employ different method to transform temporal series into 2D images
(Govindu & Palwe, 2022)	2018	"Early detection of Parkinson's disease using machine learning."	Aditi Govindu Shushila Palwe	Researchers has collected sound data from PPMI and UCI. "Its insights about jitter, shimmer and MDVP of vowel phonations" (Govindu & Palwe, 2022).	Researchers has used limited sample size and depends exclusively on audio recordings for diagnosis	Paper aim is to detect disease at preliminary stage using audio signals of PWP using machine learning method.	Audio recordings from thirty PD patients and thirty healthy volunteers were used along with ML to identify PD. Extracting features such as jitter, shimmer, and dysphonia, the researchers trained four ML models— Support Vector Machine (SVM), Random Forest, K- Nearest Neighbors, and Logistic Regression	Metrics chosen for evaluation are ROC-AUC curve confusion matrix, accuracy, precision, recall and F1 score. Highest accuracy of 91.83 % is achieved with Random Forest.	In this paper, classification of Parkinson's disease using vowel phonation data achieves 91.835% accuracy and 0.95 sensitivity with the Random Forest classifier. The Random Forest model performs exceptionally well, as it assigns equal importance to all attributes in the MDVP dataset.	outcomes , as audio signal is insufficie nt for accuratel y

Table 2 Related Research of behavioural Patten

Refrences	Year	Title	Author(s)	Dataset	Problem(s)	Purpose	Algorithms	Evaluation	Summary	Remarks
(Sangeeth a et al., 2023)	2023	"Deep Learning- based Early Parkinson' s Disease Detection from Brain MRI Image"	S. Sangeetha Dr.K. Baskar Dr Kalaivaani P.C.D T. Kumaravel,	Clinical data, image and biological data taken from PPMI website	Dataset sample was small.	Develop a model to detect Parkinson disease	CNN based method is used where number of layers are five with 16, 32 and 64 are the number of filters for first, second and last three layer, respectively. ReLU activation for each layer. Five max pooling and SoftMax layer at the end is used	Performance is measured with use of specificity, accuracy, sensitivity, and area under the curve. Classificatio n performances is having accuracy, specificity, sensitivity, and AUC of 95%, 97%, 97% and 99% respectively	In this paper, a specific CNN architecture designed with CAD is utilized to differentiate between MRI patches linked to Parkinson's disease and normal patterns. The proposed three-layer convolutional network rapidly and effectively learns patterns, thereby enhancing accuracy.	Model should be evaluated with large sample of dataset
(Xiong et al., 2023)	2023	"Auto-Classificat ion of Parkinson 's Disease with Different Motor Subtypes Using Arterial Spin Labelling MRI Based on Machine Learning."	Jinhua Xiong Haiyan Zhu Xuhang Li Shangci Hao Yueyi Zhang Zijian Wang Qian Xi	Thirty-eight subjects are enrolled in this study, including seventeen normal controls (NCs), 11 TD and 10 PIGD patients	Dataset is very small	Early detection and classificatio n of disease using model to improve the lifestyle of patients	Researcher uses a SVM method to detect PD patients using ASL-MRI data for the first time	Accuracy sensitivity, and specificity for TD patients are 84.21%, 63.64%, and 92.59%, respectively and of PIGD patients are 89%, 70% & 96.43%	The researcher has generated a classification method using machine learning to categorize ASL-MRI images of Parkinson's disease patients with various motor types and discovered that classification efficiency was particularly high in four brain regions.	Model should be evaluated on large dataset and multimodal comparative study can be included.

(Tagaris et al., 2018)	2017	"Machine Learning for Neurodeg enerative Disorder Diagnosis { Survey of Practices and Launch of Benchmar k Dataset"	Athanasios Tagaris, Dimitrios Kollias, Andreas Stafylopatis Georgios Tagaris Stefanos Kollias	dataset is having seventy-eight patients, out of which fifty-five are PD patients and twenty-three are healthy patients. Twelve patients are not having DAT-SCAN, while seven patients are not having MRI images Dataset is taken from NTUA.	Dataset has missing items and images are not of excellent quality. Retraining the DNN model can lead to unforgettable prior knowledge	The study aimed to develop deep neural networks along with it creates Parkinson's disease dataset and apply deep learning method to access and benchmark the dataset, thereby advancing the state of the art in computer-aided diagnosis (CAD) from	The DNN model used in this research is an end-to-end model that uses both CNN and RNN model. The CNNs are employed to get features from the input images, whereas the RNN leverages the sequential nature of the data to generate the final predictions.	Accuracy obtained was 99.7% on the train set and 98% on the test set.	This paper fulfils two objectives: It provides a survey of Machine Learning contributions to computeraided diagnosis and generates a new dataset. The first section reviews the key advancements in the field, while the second section introduces an innovative dataset on Parkinson's disease, which	Model should assessed large better quality dataset.	be on and of
						diagnosis			Parkinson's		

Detection of disease through voice or speech analysis, walking pattern and handwriting pattern etc. has its own challenges. It requires many variations of data like motion sequence, facial impression, or physiological indicators. It also requires combining different behavior pattern of patient like sleep pattern etc. This behavior can also be confused with aging and collecting all these data from each patient is challenging.

Many Researchers has done research on Detection of disease through MRI images. Major challenges faced by researchers is small dataset sample and inferior quality of dataset. Hence in this paper we will be using larger and better quality of dataset to train and assess the model.

1.3 Aim and Objectives

The aim of the research is to create and evaluate deep learning models for the preliminary & accurate identification and classification of Parkinson's disease using clinical and MRI image data. The purpose of the research is to diagnose and classify the disease at early stage.

The research objectives are established in alignment with the study's aim, as outlined below:

- To identify the most significant clinical and imaging features that contribute in modelling for the identification and classification of Parkinson's disease.
- To suggest an effective data balancing technique to ensure model are trained effectively and overfitting and underfitting are avoided.
- To develop machine learning models that utilize the identified features to detect Parkinson's disease and classify between tremor and PIGD.
- To evaluate the performance of the developed models in terms of accuracy, sensitivity, and specificity using cross-validation and independent test datasets.

1.4 Scope of the Study

Scope of study includes developing a tool using advanced deep learning technique on brain MRI images to detect and classify the disease at early stage. We will develop multiple models and test them on large dataset generated from PPMI website. We will evaluate our model using confusion metrics and compare our best model with some existing research work.

Study is limited to MRI images and does not include other images modalities like PET, SPECT, DTI scans etc. Dataset and models in this study doesn't include voice signal, speech behaviour, handwriting behaviour etc. The model's performance may get affected by variations in MRI machine settings and protocols across different medical centres. The study's ability to generalize the findings may get limited due to potential biases in the sample population due to social, geographical, and economic factors.

1.5 Significance of the Study

The research aims to build a methodology for preliminary diagnosis of Parkinson's disease using deep learning technique on MRI images. PD mostly goes undiagnosed until major motor symptoms (difficulty in walking, speaking, falling etc) discovers, by this time it's very late and considerable neurological damage has already occurred. Hence early detection of disease is very crucial to provide medical attention on time and control the disease effectively before it's very late and improve the lifestyle of patient. This research will contribute significantly to the area of neurology and clinical by identifying early biomarkers of Parkinson's disease from MRI images. It will provide insights into the specific brain regions and patterns associated with the early stages of PD. It will reduce the financial burden of patient by potentially reducing the long-term healthcare cost with treating advanced Parkinson's disease. Neurologist and general practitioner will benefit from a developed tool by enhancing their diagnostics method and detecting disease at early stage.

1.6 Structure of the Study

Structure of study has six chapters, each designed to systematically present the research process and findings:

Chapter 1 has introduction section, which describes background of the study in section 1.1, problem statement in section 1.2, aims and objective of project in section 1.3, scope, and significance in section 1.4 and 1.5 respectively.

Chapter 2 is a literature review section; it showcases the past results related to problems described in chapter 1 and highlights the challenges occurred while targeting the problems. It presents the review of relevant literature in the field of medical image analysis, particularly focusing on MRI-based Parkinson disease detection classification. It highlights existing approaches, their limitations, and identifies research gaps that this study aims to address.

Chapter 3 describes about dataset, dataset selection and acquisition, preprocessing of MRI image dataset, image data generator & segmentation and describes model evaluation matrix for categorical data in section 3.2. Section 3.3 describes the proposed CNN model structure and architecture in detailed manner. Overall, it is a research methodology section and describes about dataset and methodology for image classification.

Chapter 4 describes the analysis done on dataset, dataset preparation, dataset augmentation, dataset training setup and hyperparameter tuning (like batch size, learning rate, optimizer etc), implementation of proposed and pretrained model on processed dataset.

Chapter 5 describes the results of model evaluation obtained on test dataset, including performance metrics, heatmap, and comparative analysis. It also discusses the implications of the findings, limitations, and potential clinical relevance.

Chapter 6 concludes the result and findings of the study from the research and provide recommendations and suggestions regarding future scope of research. It also highlights the challenges and limitation of the study which can be taken care by future researchers.

CHAPTER 2

LITERATURE REVIEW

Parkinson's disease is an age-related degenerative brain condition, risk of developing the disease increases with age. The average age at which it starts is 60 and slightly more common in men. It deteriorates the specific part of our brain the basal ganglia and causes severe symptoms over the time. It mainly slows down the movement's tremors balance problems etc. It also effects your senses, thinking ability, mental health and more. Major motor and non-motor symptoms are mentioned in table [3]. The causes of Parkinson's disease are largely unknown, except the smaller number of inherited cases.

Table 3 Symptoms of Parkinson

	Non-Motor Symptoms		Motor Symptoms			
Loss of smell	Drooling	Constipation	Slowed movements	Tremor while muscle are at rest	Rigidity or stiffness	
gastrointestinal problems	Sleep problems	Mask like facial expression	Blinking less often than usual	Trouble swallowing	Unstable posture or walking gait	

Disease affects in multiple ways as mentioned in above paragraph. . Survey was conducted by Lisa A Uebelacker with 75 patients with Parkinson's disease with movement disorder. Question asked in the survey are, what is the two most troublesome PD related issue, what are the steps taken to cope up with the problems., which motor and non-motor problem requires the help majorly, what a comprehensive assistance program for PD patients and caregivers should include. Result of the survey says, the most problematic issues are tremor, lack of mobility pain, lack of energy, imbalance, dysarthria, and anxiety or depression. Ways to cope up with the disease are medication, physical activity, practical and emotional support. Non motor problems which needed most help is depression and anxiety. comprehensive assistance program for people with PD and their caregivers should include education, physical activity, and emotional support. National French survey was conducted by [stela] to investigate diagnosis announcement impact on huge patient with Parkinson. Survey was conducted among 39 patient, 192 caregivers and 120 healthcare. The diagnosis was not expected by about 60% of PwPD and induced negative feelings in the majority (82%) of them. Negative feelings that PwPD experience in the moment of the diagnosis announcement were related with male gender and older, while tremor as the first symptom had a threshold significance. Half of the PwPD and caregivers considered that they did not receive enough information and one third had a short-term appointment to rediscuss the diagnosis. A total of 82% of PwPD expressed the willingness to have a multidisciplinary follow-up. Only 24% of the HCPs had been trained for PD announcement. Parkinson's disease signs become more severe, expands and intensity increases as it progresses. Hence early and accurate detection of disease is very important. Practitioner uses clinical diagnosis method to detect disease as mentioned in Parkinson's foundation data. -=

We need to improve the diagnosis procedure of Parkinson patient. Hence, we need to see and understand the disease with border perspective. The definition of Parkinson's disease (PD) is changing with the expansion of clinical phenomenology and improved understanding of environmental and genetic influences that impact on the pathogenesis of the disease at the cellular and molecular level[debate]. This had led to debate and discussion with, no general acceptance of the direction that change should take either at the level of diagnosis or of what should and should not be sheltered under an umbrella of PD [debate]. The original definition by James Parkinson, and as subsequently modified by Jean-Martin Charcot, was descriptive [1]. The clinical description of PD has defined a disorder which is likely to respond to dopaminergic therapies, and this therap4utic response in turn confirms the working diagnosis. Similarly, the description

of pathology in substantia nigra, the effects of dopamine depletion in the caudate-putamen and the dramatic effects of dopamine replacement therapy demonstrated in the 1960 s have established a classical view of PD in the minds of generations of neurologists and geriatricians [2]. But with a new era of scientific discovery and more powerful investigative techniques, perhaps must come new thinking. It has led to identification of misfolded and aggregated alpha- synuclein protein, a key pathogenic feature of these disease. It has created discussion among two research groups to introduce a shift from clinical to biological shift in the definition of disease. Researchers have highlighted on the detection of alpha- synuclein as a major diagnostic tool and staging tool through lately advanced seed amplification assays, but they are following different pathways. Tanya Simuni, MD, with Northwestern University, Chicago, Illinois, proposed a biological definition that combines PD and dementia with Lewy bodies under the term neuronal alpha-synuclein disease (NSD). Definition of NSD confirms the availability of pathologic neuronal alpha-synuclein in cerebrospinal fluid (CSF), irrespective of the occurrence of detailed clinical syndrome. Patients with pathologic neuronal alpha-synuclein have high probability of dopaminergic neuronal dysfunction. Anthony Lang, MD, with the Krembil Brain Institute at Toronto Western Hospital, Toronto, Ontario, Canada, proposed the SynNeurGe biological classification of PD. These studies are not tested and evaluated by researchers. Hence practisoner cannot use this procedure on patients.

We need to address and find solution for PD motor and non- motor problem in a more realistic way. To discuss and learn more about the current and cuttingedge research behind Parkinson's disease, research conferences was conducted. Two important conference was attended by Parkinson's Canadian representative as mentioned in [Parkinson Canada] page. First was the Grand Challenges in Parkinson's conference hosted by the Van Andel Institute in Grand Rapids, Michigan. Second was International Congress of Parkinson's Disease and Movement Disorders hosted by the International Parkinson and Movement Disorder Society in Philadelphia, Pennsylvania. Broad spectrum of points was discussed in the conference, from the genetics behind PD and other movement disorders, disease modifying therapies, clinical trials, better understanding of the biology of neurodegenerative disorders, co-morbid health conditions including mood disorders and gastrointestinal issues, and more. Major discussion was to improve the understanding of how genes play a role in the development of PD. GBA1 is a gene that encodes the enzyme glucocerebrosidase, or GCase. This enzyme plays a key role in brain cell function, and mutations/disorders will cause problems where harmful substances like alpha-synuclein accumulate in brain cells, causing the characteristic cell death and dysfunction in dopamine-producing neurons that is a root cause of PD. This study was done in European ancestry and may not be applicable for other communities. Now it's very clear that there is a wide variety of mutations that can happen within genes associated with PD which affects every individual differently. Different genes affect individual differently. Dr. Lorraine Kalia researcher from Toronto is working on function that can restore endolysosomal pathway and interrupt alpha-synuclein-related neurodegeneration. Multiple studies are going on to improve neuroprotection, reduce alpha-synuclein levels in the brain via gene and stem cell therapy, and develop antibodies and immunotherapies that target alpha-synuclein specifically. Some research are going on to diagnose disease at early stage using alpha-synuclein which provides stimulation directly on specific region of brain. It is very difficult and challenging to ultimately bring these practices in market for common practices. One off the researcher from conference are working on combining physiotherapy and cognitive behavioural therapy to resolve movement disorder issue, but it's difficult to separate motor and non-motor symptoms as both are interrelated. This proves that various research addressing multiple dimensions of problem related to PD are going on across the world, but as of now most of the solution are on completed tested and cannot be implemented in the market.

Research mentioned in previous paragraph are biological, modified clinical, genetical etc. This researches are not proven or tested and clinical method are time consuming, expensive and expensive. Diagnosing the disease at early stage has become very challenging. There are other researcher groups working on creating a model to diagnose disease through voice & Speech analysis, walking pattern and handwriting pattern for fast & accurate detection and classification of disease. [Naanoue et al., 2023] has done research on detecting disease from speech analysis using deep learning. It uses Deep learning-based model using long-short term memory (LSTM) model. It detects Parkinson's disease using speech dataset of Parkinson's disease patients and healthy people. LSTM based deep, learning model is used to detect Parkinson's disease form voice signals. The mode is trained using a voice recording dataset of Parkinson disease patient and healthy patient. Confusion matrix has been created and Precision, recall, F1 score and accuracy. But problem with this research is it's not complete and accurate. (Pereira et al., 2016) has worked on diagnosing disease using handwritten dynamics. The CNN was trained through supervised learning on the dataset comprising samples from both healthy subjects and those with PD. Overall accuracy is computed using the standard formulation, i.e., (1 – errors/dataset size) *100, which is around 84-87 %. In this paper researcher has modelled handwritten data as a time series and feed it into a CNN, which can learn features to differentiate between healthy individuals and PD patients. Problem with this research is Dataset is small and not accessed on patient in the initial stages of PD. (Govindu & Palwe, 2022) has done research on detection of Parkinson's disease using audio signal through machine learning. Paper aim is to detect disease at preliminary stage using audio signals of PWP using machine learning method. Audio recordings from thirty PD patients and thirty healthy volunteers were used along with ML to identify PD. Extracting features such as jitter, shimmer, and dysphonia, the researchers trained four ML models—Support Vector Machine (SVM), Random Forest, K-Nearest Neighbors, and Logistic Regression. In this paper, classification of Parkinson's disease using vowel phonation data achieves 91.835% accuracy and 0.95 sensitivity with the Random Forest classifier. The Random Forest model performs exceptionally well, as it assigns equal importance to all attributes in the MDVP dataset. Metrics chosen are evaluation of ROC-AUC curve, confusion matrix, accuracy, precision, recall, F1 score. Highest accuracy of 91.83 % is achieved with Random Forest. Problem with this paper is Researchers has used limited sample size and depends exclusively on audio recordings for diagnosis. Many other researchers have also worked in these topics and has achieved good accuracy but it has its on challenges. It requires combination of multimodal information, variations of data like motion sequence, facial impression, or physiological indicators. It also requires combining different behavior pattern of patient like sleep pattern etc. This behavior can also be confused with aging and collecting all these data from each patient is challenging.

Hence other group of researchers has worked on creating model to Detect and classifying disease through MRI images. (Sangeetha et al., 2023) has worked on early detection of Parkinson's disease from brain MRI image using deep learning. Clinical data, image and biological data taken from PPMI website They have used CNN based method where number of layers are five with 16, 32 and 64 are the number of filters for first, second and last three layer, respectively. ReLU activation for each layer. Five max pooling and SoftMax layer at the end is used. In this paper, a specific CNN architecture designed with CAD is utilized to differentiate between MRI patches linked to Parkinson's disease and normal patterns. The proposed three-layer convolutional network rapidly and effectively learns patterns, thereby enhancing accuracy. Performance is measured with use of specificity, accuracy, sensitivity, and area under the curve. Classification performances is having accuracy, specificity, sensitivity, and AUC of 95%, 97%, 97% and 99% respectively. (Xiong et al., 2023) has researched on "Auto-Classification of Parkinson's Disease with Different Motor Subtypes Using Arterial Spin Labelling MRI Based on Machine Learning". Thirty-eight subjects are enrolled in this study, including seventeen normal controls (NCs), 11 TD and 10 PIGD patients. Researcher uses a SVM method to detect PD patients using ASL-MRI data for the first time. The researcher has generated a classification method using machine learning to categorize ASL-MRI images of Parkinson's disease patients with various motor types and discovered that classification efficiency was particularly high in four brain regions. Accuracy

sensitivity, and specificity for TD patients are 84.21%, 63.64%, and 92.59%, respectively and of PIGD patients are 89%, 70% & 96.43%. (Tagaris et al., 2018) has done research on "Machine Learning for Neurodegenerative Disorder Diagnosis Survey of Practices and Launch of Benchmark Dataset". Dataset is having seventy-eight patients, out of which fifty-five are PD patients and twenty-three are healthy patients. Twelve patients are not having DAT-SCAN, while seven patients are not having MRI images Dataset is taken from NTUA. The study aimed to develop deep neural networks along with it creates Parkinson's disease dataset and apply deep learning method to access and benchmark the dataset, thereby advancing the state of the art in computer-aided diagnosis (CAD) from medical images. The DNN model used in this research is an end-to-end model that uses both CNN and RNN model. The CNNs are employed to get features from the input images, whereas the RNN leverages the sequential nature of the data to generate the final predictions. This paper fulfils two objectives: It provides a survey of Machine Learning contributions to computer-aided diagnosis and generates a new dataset. The first section reviews the key advancements in the field, while the second section introduces an innovative dataset on Parkinson's disease, which includes epidemiological, clinical, and imaging data. Accuracy obtained was 99.7% on the train set and 98% on the test set.

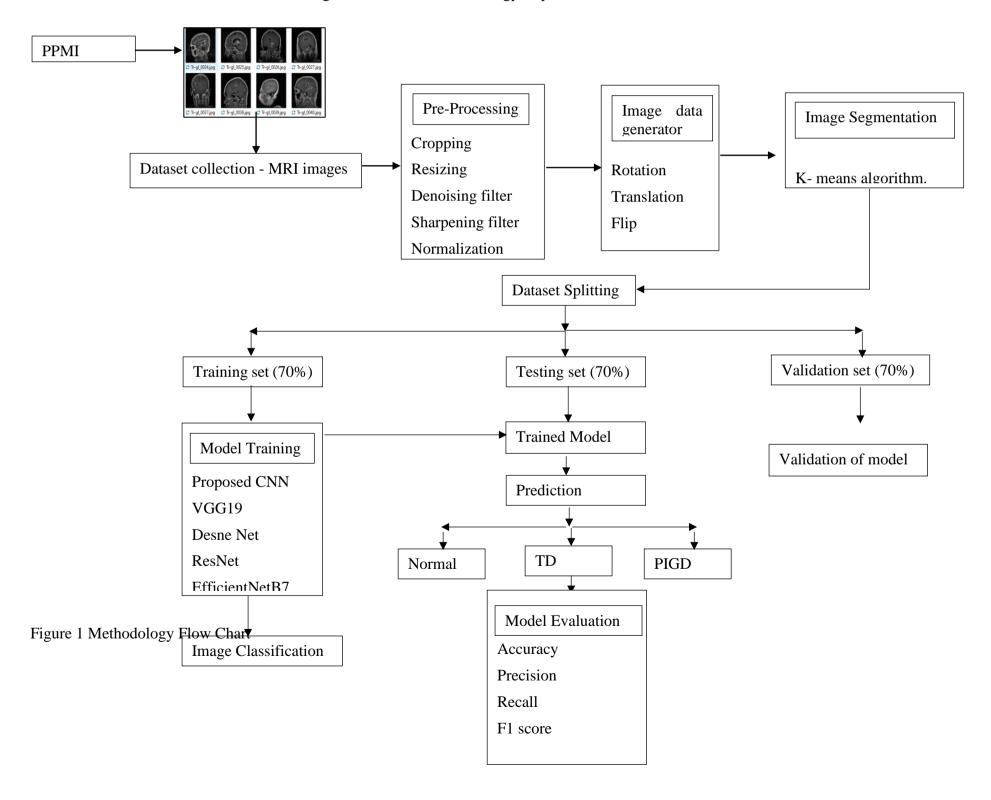
Major challenges faced by researchers is small dataset sample and inferior quality of dataset. Hence in this paper we will be using larger and better quality of dataset to train and assess the model for detection and classification of Parkinson's disease.

CHAPTER 3

METHODOLOGY

3.1 Introduction

It explains the methodology used to detect and classify the model and evaluate classification model. Detection and classification of Parkinson using MRI images goes through multiple steps like acquiring proper dataset, image preprocessing, image filtering, image augmentation, image segmentation & feature extractor, CNN model and data evaluation. Figure 1 shows the methodology steps taken for this research.



3.2 Dataset Acquisition

Dataset utilized in the study is downloaded from Parkinson's Progression Markers initiative i.e., PPMI website (http://www.ppmiinfo.org). We need to apply for the access to use or download dataset). "PPMI aims to identify biological markers of Parkinson's risk, onset and progression (About PPMI, 2010)". Website contains 2614 female, 2758 male and 2 unknown number of patient data as shown in Table 3.1. It has 393 healthy, 1684 Parkinson's disease (PD), 81 SWEDD, 3207 Prodromal and 19 AV133 patient record as mentioned in Table 3.2. MRI images can be downloaded from "download" section of website. We are using 832 images of PD patient record having tremor (571) and PIGD (261) subtype of Parkinson's disease and 200 images of healthy patient. We are using images recorded in Siemens's lab having weighting PD, T1 and T2. PD patient having tremor and PIGD subtype Parkinson's can be filtered from excel ("PPMI Curated Data Cut Public 20240129-1.xlsx") in Study data section of website.

Table 4 Gender of Patient

Gender	No of Patient
Male	2758
Female	2614
Unknown	2

Table 5 Types of Patients

Patient Type	No of Patient
Healthy	393
PD	1684
SWEDD	81
Prodromal	3207
AV133	19

3.3 Image Preprocessing

MRI scan raw images needs to be pre-processed before using it for modelling for better accuracy. Images will be of different shape, size formation and quality, to standardize the quality we need preprocessing. Images preprocessing steps includes multiple steps. Image is first passed through cropping function which crops the main parts of the image. We need to resize the image to fixed size after cropping, then first filtering method is applied to reduce the noise of the image

using median filtering, second filtering method is applied to sharpen the image and improve brightness using OpenCV2's Laplacian. Last step is to use normalization to re-scale image to range of 0-1 to ensure all features have similar scale.

3.4 Image data generator and segmentation

Data is split into train set (70%) and test set (30%). We applied data transformation like rotation, translation, flip, zoom, brightness adjustment etc to diversify and expand the training dataset. It improves model generalization and simulates real world scenario as in real world image can be in any formation. Later we need to segment the image using k-means algorithm by a value of K to divide an image into meaningful segments based on pixel intensity, colour, texture etc. Last, we need to rescale the training image data and test data. We don't apply data augmentation on test data, only rescaling of data is required.

3.5 Model Evaluation

We will evaluate the different models of this research using different metrics.

- ROC-AUC: The performance of a binary classification model is evaluated using metrics. It has overall ability to discriminate between positive and negative classes. It stands for are under ROC curve.
- Accuracy: It is measure of overall correctness of model, number of correct predictions out all the prediction. It is very useful when the classes are balanced and very misleading when dataset is not balanced.
- Precision: It is known as Positive Predictive value and measures accuracy of positive prediction. It indicates the number of actual predicted positive out all the positive prediction. It is required where false positive is very important.
- Recall: It is known as True Positive rate and evaluates the ability to acquire all positive cases. It is required where false negative is very important.
- F1 score: It is the harmonic means of Precision and recall, single metrics which balance both precision and recall. It is important when both false positive and false negative is important.

Formula of all these test parameters is mentioned in Table 3. We will also compare our best model with different model generated by existing research work based on MRI images mentioned in related work of table 2. We will also compare our model with existing research work done based on voice signals, speech analysis and handwriting behaviour as mentioned in related work of Table 1.

Table 6 Evaluation Matrix

S.No.	Metrics	Formula
1	Accuracy	True positive + True Negative × 100%
		True Positive + True Negative + False Negative + False Positive $\stackrel{\times}{\sim}$ 100%

2	Precision	True Positive × 100%
		$\frac{100\%}{True\ Positive + False\ Positive} \times 100\%$
3	Recall	True Positive
		$\overline{True\ Positive + False\ Negative} imes 100\%$
4	F1 score	Precision × Recall
		${Precision + Recall} \times Z$

3.6 Feature Extractor and model classification

Feature extractor identifies and extracts important feature, which can be used for classification. It tries to minimize the amount of data and preserves valuable information. Deep learning models receives pre-processed MRI images as input and labels it as Healthy (HC), Tremor (TD) and PIGD. CNN model comprises of 4 convolution layer and 32 filter for first layer ,64 filter for second layer and 128 filter for last layer. Convolution network uses 2D kernels of [3X3] to transform them into feature map such as edges, texture etc. and ReLu function was used as activation layer for convolution network. ReLu activation function provides non-linearity to model while keeping the computation simple and efficient Four max pooling layer is used to reduce the dimension of feature map and retains the valuable information of the image. There is one flatten layer between last max pooling and dense layer to transform multidimensional output into a one-dimensional vector. We have 2 dense layer and one-dimensional vector goes as an input to this layer. Dense layer network is responsible for final classification model as HC, PD and PIGD uses Soft Max activation function. Batch Normalization is added for first three layer of convolution neural network. CNN model architecture is given in figure 2. Data is then fed into network for training, testing and validation. We will also use multiple pre -trained model like VGG19, Dense Net, ResNet and EfficientNetB7 on the same dataset to compare the performance of model and identify the best model for this research. Classification and detection of disease are modelled separately using same CNN model architecture.

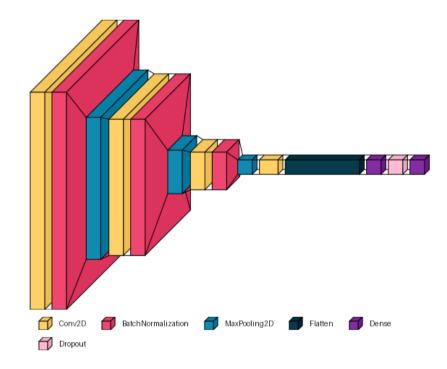


Figure 2 CNN Model Architecture

3.7 Summary

The project aims to a model to detect and classify image using deep learning techniques. The methodology was designed to ensure high accuracy and efficiency in recognizing and categorizing images. The dataset used for this is from PPMI website and multiple preprocessing technique is applied to improve efficiency and overfitting. CNN architecture and pre trained model is used as they are efficient in image classification technique.

Chapter 4

ANALYSIS AND DESIGN

4.1 Introduction

Chapter shows the analysis and design of proposed classification model for MRI image detection and classification. The analysis phase involves understanding the dataset, system required to run classification model, selecting efficient and accurate methodologies to train and evaluate the model. System was designed using deep learning-based convolution Neural Network technique. Architecture is consisting of multiple layers to extract feature from images. Other section of this chapter describes system requirements, data analysis, architectural design of image classification.

4.2 Dataset Preparation

Dataset downloaded from PPMI website is in DICOM format having dcm extension. Dataset is first converted to usable png format. Dataset is divided between Classification of disease and detection of disease. Classification of disease dataset is classified into three categorical classes Tremor, gait Disability and Healthy subtypes. Detection of disease dataset is classified into two categorical classes Disease and Healthy subtypes. Dataset is imported into python notebook and number of trainings and testing data path/label is calculated. Classification of disease Dataset is divided between Training and test data having three categorical classes of patient Tremor gait Disability and Healthy as shown in Figure 3. Detection of disease Dataset is divided between Training and test data having two categorical classes of patient Disease and Healthy as shown in Figure 4. Image is converted to target size required for modelling for example (150,150) for CNN model, reshaped to (150,150,3) format and then finally normalized to get data in same standard. A sample image is displayed to visualize its appearance as shown in Figure 5.

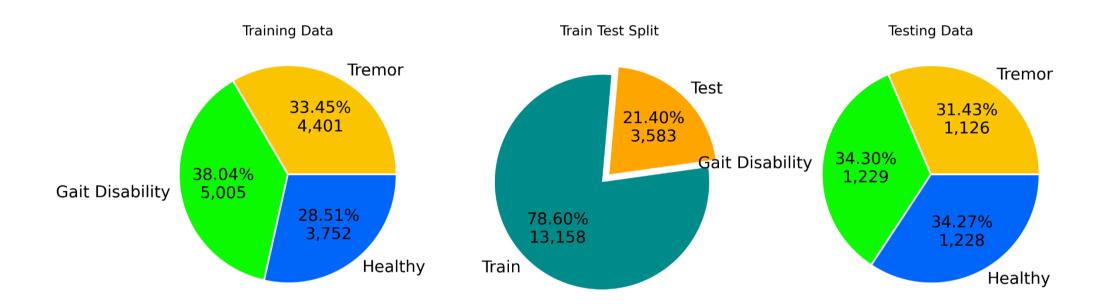


Figure 3 Classification of Disease Dataset

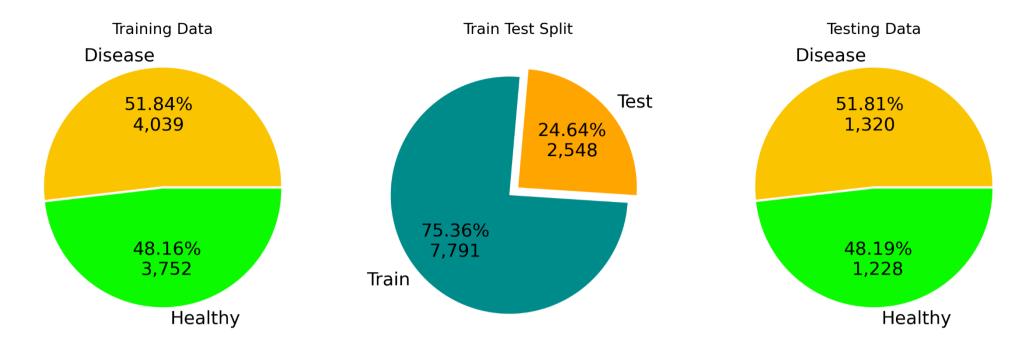


Figure 4 Detection of Disease Dataset

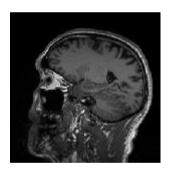
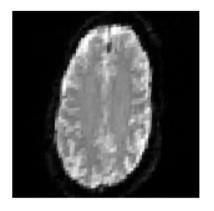
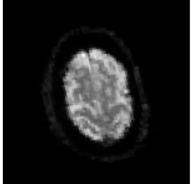


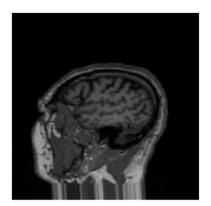
Figure 5 Sample Image

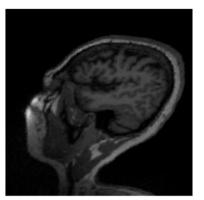
4.3 Data Augmentation

Data augmentation is applied to the training data, including rescaling, 10-degree rotation, brightness adjustment (0.85 to 1.15), width and height shifts (0.002), shear transformation, 0.2 zoom, and horizontal flipping. Data augmentation is not applied to the test data only rescaling is performed. Categorical class Tremor, gait Disability and Healthy for classification of disease and Healthy and Disease is converted to numerical index. The augmented training data is visualized to observe the applied transformations as shown in Figure 6.









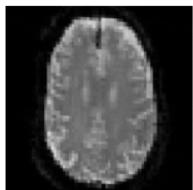


Figure 6 Augmented Image

4.4 Training Data Setup and Hyperparameter tuning.

Training data shape, batch size, Number of epochs, training steps per epoch, validation steps per epoch is defined and calculated before each model. Modelling methods used for classification of disease in the project are CNN model, DenSet and ResNet. Modelling methods used for detection of disease in the project are only CNN.

4.4.1 Conventional CNN

CNN architecture used multiple layers of convolution network and 2d max pooling with one fully connected layer, detailed structure is mentioned in Figure 7. Convolution network uses Adam optimizer with learning rate of 0.001 and categorical cross entropy as loss calculation during compilation. Several callbacks, including a learning rate scheduler, early stopping, and reduce learning rate on plateau, were implemented. The learning rate scheduler, with a factor of 0.9, reduced the learning rate by 10% after each epoch. Early stopping was applied to prevent overfitting, stopping training if the loss variation between consecutive epochs was less than 1e-9. Reduce learning rate on plateau callback reduces the learning rate if validation loss doesn't improve for several epochs with the factor 0.3%. Training data was then sent to convolution neural network model in different batches and for different epochs to get required results. Optimized batch size, training step per epoch, test steps per epoch and number of epochs were selected after multiple iteration. The model's accuracy doesn't change significantly after a certain epoch as shown as example in Figure 8, leading to overfitting. Therefore, selecting the appropriate number of epochs is crucial. Same model architecture and optimizer etc. has been used for both classification and detection of disease. Difference in both the modelling methods are two hyperparameter batch size and learning rate.

Model: "sequential_51"

Layer (type)	Output Shape	Param #
conv2d_204 (Conv2D)	(None, 148, 148, 32)	896
<pre>batch_normalization_153 (B atchNormalization)</pre>	(None, 148, 148, 32)	128
<pre>max_pooling2d_153 (MaxPool ing2D)</pre>	(None, 49, 49, 32)	0
conv2d_205 (Conv2D)	(None, 47, 47, 64)	18496
<pre>batch_normalization_154 (B atchNormalization)</pre>	(None, 47, 47, 64)	256
<pre>max_pooling2d_154 (MaxPool ing2D)</pre>	(None, 15, 15, 64)	0
conv2d_206 (Conv2D)	(None, 13, 13, 128)	73856
<pre>batch_normalization_155 (B atchNormalization)</pre>	(None, 13, 13, 128)	512
<pre>max_pooling2d_155 (MaxPool ing2D)</pre>	(None, 4, 4, 128)	0
conv2d_207 (Conv2D)	(None, 2, 2, 256)	295168
flatten_51 (Flatten)	(None, 1024)	0
dense_102 (Dense)	(None, 12)	12300
dropout_51 (Dropout)	(None, 12)	0
dense_103 (Dense)	(None, 3)	39

Figure 7 CNN Architecture

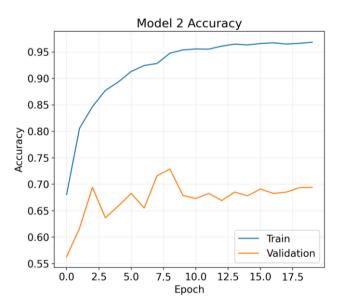


Figure 8 Accuracy Epoch chart

4.4.2 Dense Net Model

Densely connected convolution network is pretrained deep learning model architecture. We have used dense Net model to get better results as it is a proven architecture. Dense Net uses image size of 224X224, image is first converted to appropriate size, then reshaped and squeezed into required format. MRI grayscale scan will be converted into 3 channel format and then normalized and displayed as shown in Figure 9.

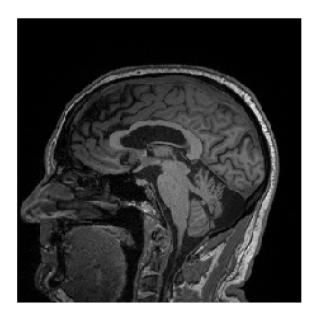


Figure 9 Dense Net MRI image

The base model architecture was modified before using it for modelling. DenseNet121 has been used to model the image with ImageNet weight. The base model layers were frozen, and a Global Average Pooling layer was added to the base layer's output. A densely connected layer with 512 filters, kernel regularization, and ReLU activation was incorporated. Batch normalization was performed to normalize the data, followed by the addition of a dropout layer. Another dense layer with 256 filters and sigmoid activation was included, followed by another dropout layer. Predictions were made using the train generator classes with soft max activation. The first 300 layers of the architecture were unfrozen for training.

The Adam optimizer with a learning rate of 0.001 and categorical cross-entropy was used as the loss function during model compilation. Several callbacks, including a learning rate scheduler, early stopping, and reduce learning rate on plateau and model checkpoint were implemented. The learning rate scheduler, with a factor of 0.9, reduced the learning rate by 10% after each epoch. Early stopping was applied to prevent overfitting, stopping training if the loss variation between consecutive epochs was less than 1e-9. Model check point save weights of a model for every epoch in a provided path for future calculation and reference. Training data is sent to model architecture in different batch size and epoch to get efficient and accurate result. Optimized batch size is selected to give good training and test accuracy result. Optimal epoch is selected to avoid overfitting of model based on Figure 10 graph.

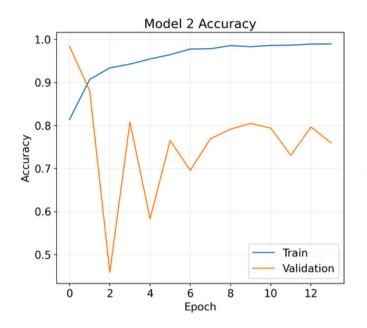


Figure 10 Dense Net model accuracy graph

4.4.3 ResNet Model

Residual network in a pre-trained deep learning architecture. Along with Dense Net, the ResNet model has also been used for disease detection and classification. ResNet uses image size of 224X224, image is converted into appropriate size, reshaped, and squeezed into required form. Image is preprocessed to ResNet Model requirement, and displayed as shown in Figure 11

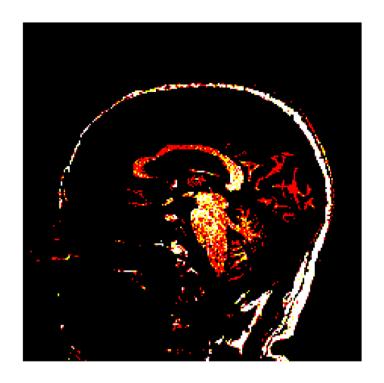


Figure 11 Resnet MRI image

The base model architecture was modified before applying it to image data. ResNet50 has been used to model the image with imagenet weight. The base model layers were frozen, and a Global Average Pooling layer was added to the base layer's output. A densely connected layer with 512 filters, kernel regularization, and ReLU activation was incorporated. Batch normalization was performed to normalize the data, followed by the addition of a dropout layer. Another dense layer with 256 filters and sigmoid activation was included, followed by another dropout layer. Predictions were made using the train generator classes with soft max activation. The first 50 layers of the architecture were frozen and except first 50 layers are trainable.

The Adam optimizer with a learning rate of 0.001 and categorical cross-entropy was used as the loss function during model compilation. Several callbacks, including a learning rate scheduler, early stopping, and reduce learning rate on plateau and model checkpoint were implemented. The learning rate scheduler, with a factor of 0.9, reduced the learning rate by 10% after each epoch. Early stopping was applied to prevent overfitting, stopping training if the loss variation between consecutive epochs was less than 1e-9. Model check point save weights of a model for every epoch in a provided path for future calculation and reference. Training data is sent to model architecture in different batch size and epoch to get efficient and accurate result. Optimized batch size is selected to give good training and test accuracy result. Optimal epoch is selected to avoid overfitting of model based on Figure 12 graph.

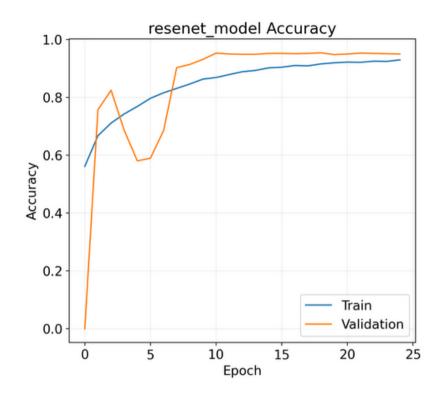


Figure 12 ResNet model Accuracy graph

4.5 Summary

Detection and classification of model is implemented on same CNN architecture model. Further for of model ResNet, and DenseNet has been used. Hyperparameter (learning rate, batch size, optimizer) tuning has been done while modelling dataset of Parkinson disease detection and classification.

CHAPTER 5

RESULT AND DISCUSSION

5.1 Introduction

Results obtained from the proposed MRI image classification and detection model is discussed in this section. Model has been evaluated and validated using various parameter accuracy, Precision, recall, F1-score, and confusion matrix. Result obtained from pre-trained model has also been discussed and compared with proposed model architecture.

5.2 Validation Dataset Test Result

The proposed CNN architecture has been tested on Parkinson MRI images. The test result obtained from Validation dataset of Disease detection shows accuracy of 78%, Precision of 80%, Recall of 77.1% and F1score of 80% and results are presented in the Table 4 and Disease Classification shows accuracy of 50%, Precision of 41%, Recall of 53% and F1score of 45.5% and results are presented in the Table 5. Accuracy of disease detection model is low compared to benchmark dataset given by Tagaris et al., 2018. Benchmark dataset achieved the accuracy of 98% but sample size of dataset is very small, and we have experimented on larger dataset, and dataset image quality is not adequate.

Table 7 Disease Detection metrics

Metric	Healthy (%)	Disease (%)
Accuracy	78	
Precision	81.8	76.4
Recall	71.7	85.2
F1-Score	76.4	80.5

Table 8 Disease classification metrics

Metric	Healthy (%)	Gait Disability (%)	Tremor (%)
Accuracy	50		
Precision	71.2	11.6	41.7
Recall	62.9	7	90
F1-Score	66.8	12	57.7

Confusion matrix of disease detection in Figure 14 shows that the model correctly classified 1124 out of 1471 patient with Parkinson disease and 881 out of 1071 healthy patients.

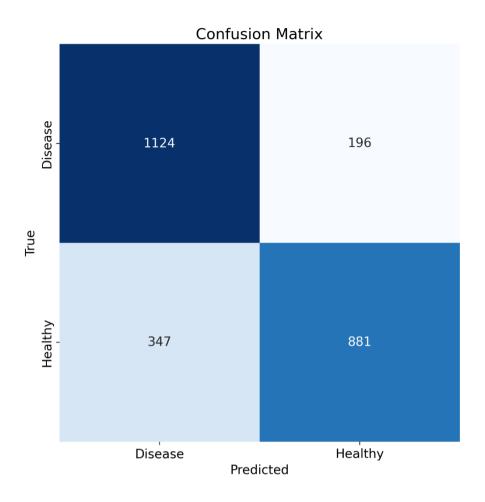


Figure 13 Confusion Matrix of disease detection.

Confusion matrix of disease detection in Figure 14 shows that the model correctly classified 772 out of 1228 patient healthy and 1013 out of 1126 patients as Tremor subtypes and 8 out of 12299 patients as Gait Disability. Misclassifications were primarily near patients with Gait Disability. This is majorly because tremor and Gait Disability subtypes is not related to brain, rather it has behavioural difference. Hence model is not able to classify between tremor and Gait disability subtypes of Parkinson disease.

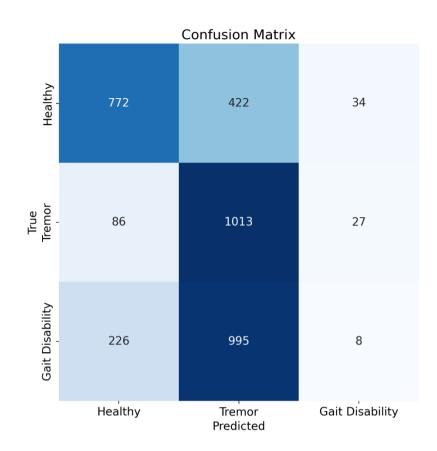


Figure 14 Confusion Matric of disease classification

Proposed CNN model architecture has been compared with two pre trained model Dense Net and ResNet. Dense Net and ResNet has been modified and trained on same dataset as of proposed model and results are compared. Comparison results for disease detection and classification are tabulated in Table 5. Pretrained model is have shown improvement in accuracy, which proves that model will achieve good accuracy if tested with better quality of image and combined with behavioural pattern dataset.

Table 9 CNN model Vs pretrained model

Model	Disease Detection Accuracy (%)	Disease Classification Accuracy (%)
CNN Model	78	50
ResNet Model	82	70
Dense Net Model	558	60

ResNet Model accuracy is 82 and 70% in disease detection dataset and disease classification dataset respectively. ResNet model has achieved a=higher accuracy which shows that model accuracy will be improved after slight change in base model. Dense Net model accuracy is 58% and 60% in disease classification dataset respectively.

5.3 Validation data Result Discussion

Misclassifications were primarily near patients with Parkinson patients in Figure 14. This is majorly because MRI images dataset is not in consistent format, it has different orientation like axial, coronal, and sagittal views. Additionally, some MRI samples contained a single slice, while others included multiple slices or full 3D volumes, leading to variation in input dimensions. Differences in resolution, contrast levels, and the presence of artifacts or noise further contributed to data heterogeneity, potentially impacting the model's ability to learn consistent and discriminative features."

Model achieved accuracy of 80% in Parkinson disease detection, but it fails to achieve decent accuracy in model classification. Proposed model is not able to find major difference in the MRI images of Gait Disability and Tremor patients. Parkinson is a neurovegetative disorder where neurons in the midbrain that produce dopamine dies, but this is common for both Gait Disability and Tremor subtypes of Parkinson. Major difference between two subtypes is not related to brain, rather it has behavioural difference. Hence while detecting disease, model was able to find some pattern in the MRI images of patients with Parkinson and without Parkinson disease but failed to classify between Gait Disability and Tremor during Disease classification. Hence to detect and classify the model accurately we need to combine MRI images data along with, behavioural data like handwriting pattern, voice pattern, walking pattern etc. Scope of the project was to test only with MRI images; hence we have not combined behavioural data with MRI images.

5.4 Summary

The results demonstrate that our CNN model is effective for MRI-based Parkinson disease detection, but better quality of data in consistent format required to enhance the result. Classification of disease should be tested on behavioural data along with MRI images like handwriting pattern, voice pattern, walking pattern etc.

CHAPTER 6

CONCLUSION AND RECOMMENDATION

Study has focused on developing a Convolution neural network model to detect and classify Parkinson disease using MRI images. Proposed CNN architecture has achieved 80% accuracy on validation data of disease detection, but accuracy is 50% on validation data of disease classification. Model has been tested with multiple combination of batch size, learning rate, kernel size, dropout algorithm.

In clinical terms, the model could serve as a decision support tool for radiologists by flagging potential Parkinson cases with high sensitivity, thereby reducing diagnostic oversight. To enhance real-world application, future work will focus on:

- Expanding the dataset with more diverse of MRI scans
- Incorporating better quality of data
- Incorporating consistent format of data
- standardizing MRI data formats and orientations to ensure consistency during training and inference.

Model classification performance should be tested and evaluated with combination of MRI images and behavioural or clinical data, before confirming its clinical applicability to ensure comprehensive and reliable decision-making,

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