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Analysis of Parkinson's Disease Data

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Abstract

In this paper, we investigate the diagnostic data from patients suffering with Parkinson's disease (PD) and design classification/prediction model to simplify the diagnosis. The main aim of this research is to open possibilities to be able to apply deep learning algorithms to help better understand and diagnose the disease. To our knowledge, the capabilities of deep learning algorithms have not yet been completely utilized in the field of Parkinson's research and we believe that by having an in-depth understanding of data, we can create a platform to apply different algorithms to automate the Parkinson's Disease diagnosis to certain extent. We use Parkinson's Progression Markers Initiative (PPMI) dataset provided by Michael J. Fox Foundation to perform our analysis.

Keywords: Parkinson's, Unified Parkinson Disease Rating Scale (UPDRS), convolutional neural network (CNN), Long Short Term Memory (LSTM)

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1. Introduction

Recent work has shown that deep learning algorithms can be successfully applied in medical field for various detection and prediction tasks. Many of these works include the use of convolutional neural networks (CNNs) for brain segmentation, tumor detection and diabetic retinopathy [1-6]. In addition to CNNs, long short-term memory (LSTM) algorithms were also used for general diagnosis of diseases [7-8]. These applications have shown that with a proper collaboration between healthcare and deep learning researchers, we can create a pipeline for easier and faster diagnosis of diseases.

In this paper, we investigate the challenges faced in Parkinson's disease diagnosis and discuss the possibilities of using deep learning algorithms. Parkinson's disease (PD) is a chronic, progressive and neurodegenerative disease caused by the loss of a neurotransmitter called dopamine in the substantia nigra of the brain. Fig 1 shows the location of substantia nigra in the brain and also the substantia nigra between a healthy subject and a PD patient. Usually, PD is more common in the elderly population, producing alterations in gait and posture that may increase the risk of falls and lead to mobility disabilities. As such, it impacts daily activities and reduces the quality of life concerning patients and their families [9].

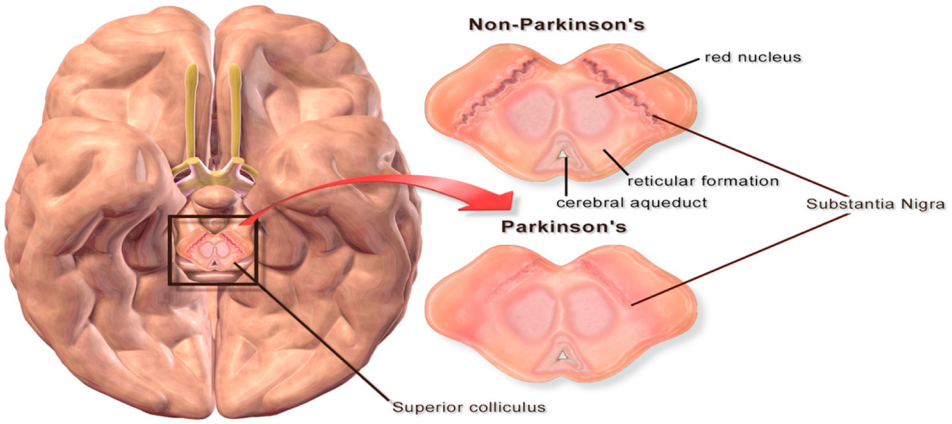

Fig 1 : Image showing substantia-nigra between healthy subject (top right) and PD patient (bottom right)

The symptoms of PD generally develop over years. The progression symptoms are usually different from person to person due to the diversity of the disease. This makes the diagnosis of the disease in the early stages extremely difficult. The present diagnosis of the Parkinson's disease is predominantly clinical; however, imaging helps to confirm dopamine degeneration and also to differentiate between Parkinson's disease and atypical parkinsonism [10]. In addition, the severity of the disease is also measure using Unified Parkinson Disease Rating Scale (UPDRS) which contains the record of various patient movements recorded at regular intervals.

By understanding how the imaging and UPDRS data is used for PD diagnosis and research, we can formulate problems that uses the capabilities of deep learning and reduce the manual effort spent to analyze this data. Since there is no established approach to confirm the PD, doctors use multiple tests and imaging to confirm the disease. We present an overview of different types of data used and create a classification/prediction problem to simplify the diagnosis.

Like any other deep-learning application, training of algorithms for medical applications also requires significant amount of labelled data [19]. In case of medical imaging, the data should include the labels of the particular diagnostic

element that we are interested to predict/classify [19] while LSTM models require time-series type data [7-8]. By identifying type of data used for PD diagnosis, we define which parameters have to be manually labelled for image data and which features can possibly be used for time-series data. Additionally, we define how to evaluate the performance parameters for the trained algorithms to validate the results.

2. Abbreviations

PD: Parkinson's Disease
IPD: Idiopathic Parkinson's Disease – confirmed PD.
APD: Atypical Parkinsonism – having symptoms of PD
PSP: Progressive Supranuclear Palsy – case of APD
MSA: Multiple System Atrophy – case of APD
CBD: Cortico Basal Degeneration – case of APD
UPDRS: Unified Parkinson Disease Rating Scale
MDS: Movement Disorder Society - Unified Parkinson Disease Rating Scale
CNN: Convolutional neural network
LSTM: Long short-term memory

3. Related Work

Neural networks have been applied to medical problems for more than a decade. However, with the improvement of computational power in recent years, deep learning algorithms such as CNN's found their way into medical field with their high accuracy in detecting tumors and other abnormalities [1-5]. The most notable CNN application for tumor detection involve classifying each voxel in an MRI whether it is an infected or not. The performance is measured using dice coefficient where the classified MRI images were compared with ground truths to calculate the accuracy of the architecture. Similar applications are done for the diagnosis of diabetic retinopathy [6]. In case of PD, the medical imaging includes the use of multiple scans such as MRI, PET and DAT-scan where each scan should have its own trained models to be able to useful in PD diagnosis.

LSTM's are well suited to predict time series given time lags of unknown size and duration between important events. Although there are no significant applications of LSTM's for medical data, there are a few cases where they were used to predict clinical events [7], heart failures [8] and rice blast disease [21]. In case of UPDRS data, which mainly contains the record of the disease for a PD patient over the years, LSTM's can be trained to predict how the disease progresses for different types of medications.

As per our knowledge, there is very little research done with respect to Parkinson's using deep learning algorithms. In "Deep Learning-Aided Parkinson's Disease Diagnosis from Handwritten Dynamics" [20], the authors used hand-written dynamics to diagnose the disease. Since Parkinson's is a neuro-degenerative disease, the dynamics of the characters written can help to understand the severity of the disease. In "Deep learning Parkinson's from smartphone data" [17], the authors used smartphone data to predict the progression of the disease using different machine learning algorithms. However, the diagnosis of the disease involves multiple features which include motor functions, dopamine concentration and many other clinical tests. Therefore, using only one feature to understand the disease is not enough as there is multiple brain related diseases with similar symptoms.

4. Analysis of Parkinson's Data

Our research is presently at the intersection of deep learning and Parkinson's disease. While we cannot provide completely automated designs to automate the diagnosis of Parkinson's disease, we intend to simplify the process using trained deep neural networks.

4.1. Imaging for Parkinson's

Research shows that the error rate for the diagnosis of PD can be as high as 24%, even at specialized centers [9]. Most of these misdiagnoses include atypical parkinsonian disorders (APDs) such as progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD). Brain structural imaging using different types of MRI is normally used to detect or rule out underlying pathologies causing parkinsonism.

A case study was done in [12] where they were able to successfully differentiate the cases of PSP, MSA and CBD using just the MRI. However, in cases of idiopathic Parkinson's, MRI alone was not enough to diagnose the disease. In a similar way, a lot of research was done to find imaging biomarkers from MRI which can help diagnose idiopathic Parkinson's.

While MRI have proved to be useful to some extent in diagnosing PD, they are not sensitive enough to detect the volumetric changes in substantia-nigra. For this purpose, PET and SPECT are preferred as they provide in-depth images of the structure of substantia-nigra. Fig-3 shows the dopamine levels of a healthy subject and a patient with Parkinson's disease. The decreasing volume of substantia-nigra indicate the stage of the disease at different time periods. Even though PET and SPECT scans prove to be more useful than MRI, they are not generally preferred as the first step of diagnosis considering the side-effect and price.

Swallow Tail segmentation of MRI

In case of PD, the loss of substantia nigra dopaminergic neurons is most prominent sub-regions called nigrosomes. It was shown in [11] that high-resolution, iron-sensitive, magnetic resonance imaging (MRI) at 7T allows direct nigrosome-1 visualization in healthy people but not in PD. The healthy nigrosome-1 on high-resolution 3T – SWI will show a swallow tail appearance while it becomes less dominant in case of PD patients depending on severity. Fig 2 shows the swallow tails for a healthy subject and a PD patient.

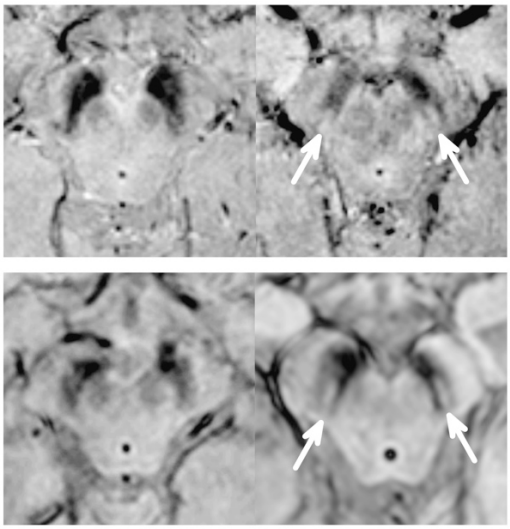

Fig 2: MRI showing the absence of swallow tail in top left and bottom left patients with PD. The top right and bottom right are non-PD patients with clear swallow tails. Image modified from the 'swallow tail' appearance of healthy nigrosome – A new accurate test of Parkinson's disease: A case-control and retrospective cross-sectional MRI study at 3T [11].

The application of CNN for sallow tail segmentation includes accurate classification of each voxel in the MRI to get the exact shape of the swallow tail. In cases where PD is confirmed and to understand how well the patient is responding to dopaminergic therapy, an accurate segmentation will be useful to analyze the progress.

Volumetric segmentation of dopamine

When the diagnosis of PD is not clear using MRI and other clinical test especially when considering potential risky procedures like deep brain simulation, it is often recommended to use PET or SPECT scan [10,13]. It is an invasive approach where the imaging agent is injected and the compound will be visualized under specialized gamma cameras which measures the dopamine transporter (DaT). Fig 3 shows the PET scan between a health subject and a PD patient. We can clearly observe the reduced dopamine volume for PD patients.

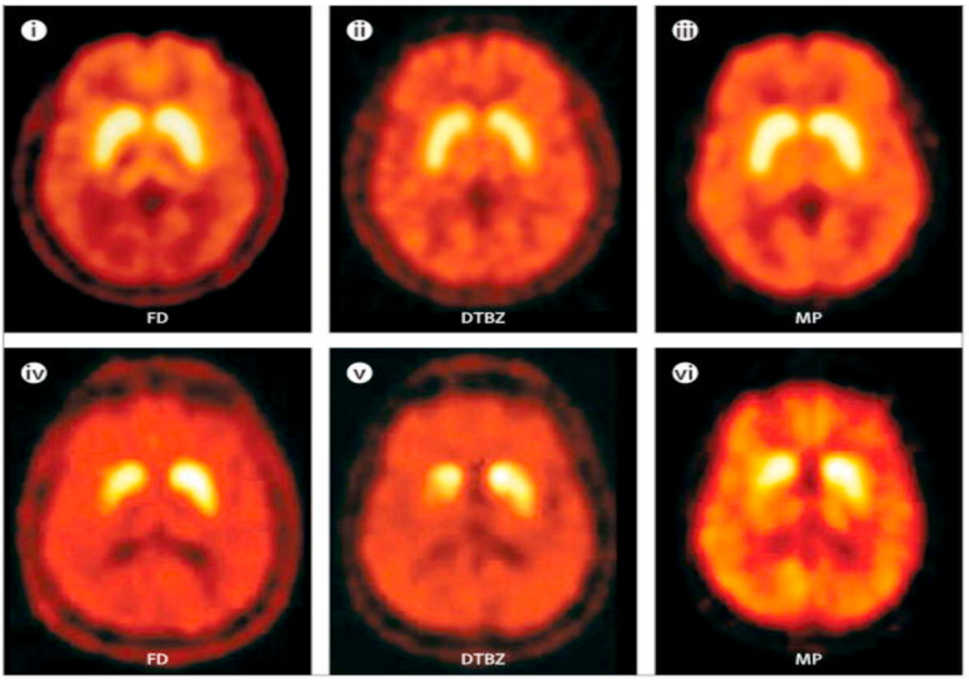

Fig 3 : PET images from a healthy individual (I - iii) and a patient with mild Parkinson's disease (iv - vi). Image modified from Imaging insights into basal ganglia function, Parkinson's disease, and dystonia [10].

In order to use CNN's for the segmentation of dopamine concentration, a volumetric approach is required [18] as the total volume of dopamine defines the state of the disease [22]. The training of CNN architecture should include frame by frame classification of pixels to get the total volume. The measurement of accuracy can simply be done using dice coefficient by comparing the results with ground truths.

Volumetric segmentation of white and gray matter

In addition to monitoring the dopamine degeneration in substantia nigra, researchers are actively trying to find other relationships with Parkinson's disease [12,14-16]. In recent years, there is evidence of cerebral atrophy (i.e. reduction in gray matter) for patients with dementia in Parkinson's disease [14]. The segmentation of white and gray matter also requires trained CNN's capable of classifying each voxel in the MRI frame by frame to get the total volume of the white and gray matter.

4.2. LSTM for Parkinson's data

Severity of Parkinson's is usually assessed by Unified Parkinson Disease Rating Scale (UPDRS) [23]. After several revisions, the present established scale is called MDS-UPDRS [24-25] which is published by Movement Disorder Society (MDS). The MDS-UPDRS consists of 4 parts:

1. Mentation, Behaviour and mood
2. Activities of daily living
3. Motor examination
4. Complications of therapy

Table 1 shows a sample of UPDRS data over the span of 4 years for a patient. The data shows how the patient is responding to the treatments over the years. We can correlate this data with that of time series data as each point is set in time order. The challenging part of using LSTM in this context is to identify which features should be used to predict the progression of the disease. The table shows only 4 features for simplicity, however, the real UPDRS data has more than 30 features just for the case of arm-swing. By identifying the features which can accurately define the disease, the LSTM will have the possibility to develop progression paths for patients. However, since the exact cause of PD is unknown, a collaboration between neurologists and deep learning researchers is required to decide on which features to use.

Table 1. An example of a UPDRS record. Data taken from Michael J. Fox Foundation's PPMI dataset.

PATNO	EVENT_ID	INFODT	COHORT	SP_U	RA_AMP_U	LA_AMP_U	RA_STD_U
42415							
	V06	Dec-14	3	1.138	12.45788542	31.33219988	2.235029724
	V04	Jun-15	1	0.994	30.5852388	38.06316559	5.048072162
	V04	Nov-15	3	0.996	17.19155094	29.27368362	2.70208348
	V04	Jan-16	3	0.881	7.695238284	3.838619168	2.113256137
	V04	Jun-16	3	1.049	32.94379154	33.37457256	5.813496009
	V08	Jan-17	3	0.909	37.97438713	44.10466383	7.701399724
	V08	Nov-17	3	1.163	13.30896589	12.13666854	2.039650937

4.3. Segmentation with UPDRS

A significant amount of deep learning research involves using CNN and LSTM's together to perform tasks such as image captioning and video tagging [19]. In a similar setting, it becomes possible to use imaging data together with UPDRS data to generate the progression paths for the disease. However, this becomes possible only once it is established that CNN and LSTM gives high accuracies on segmentation and UPDRS data respectively.

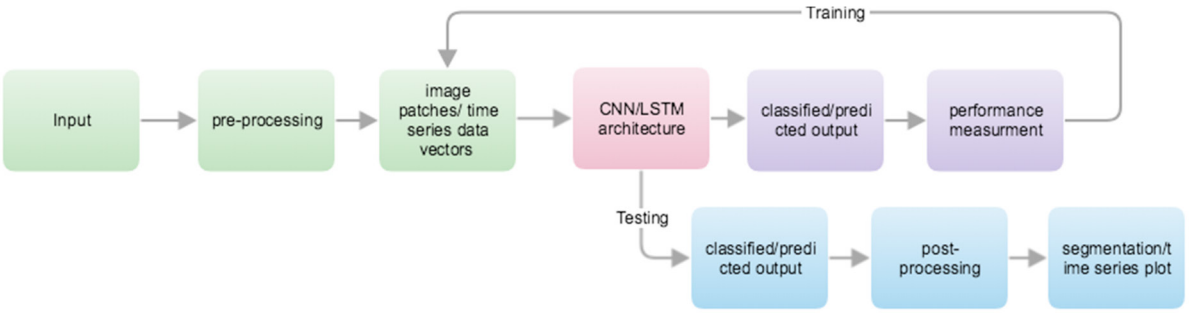

Fig 4: Workflow for Parkinson's net architecture

5. Conclusion and Future Work

In this paper, we discussed the various possibilities of using deep learning algorithms in the field of Parkinson's research. We described which type of segmentation should be used for different imaging techniques and how UPDRS data can be used with LSTMs to give the progression of disease. Using this as foundation, we plan to train different CNNs and LSTMs to show how the deep learning algorithms can be used to analyze the Parkinson's data.

So far, we were able to generate initial segmentation of substantia nigra using the work flow shown in Fig 4. Our approach involves generating patches from input scans which are fed into a CNN architecture to classify whether the center pixel in the patch belongs to substantia nigra or not. These findings will be released in a paper in the near future.

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