Determining Brain Imaging Biomarkers for Parkinson's Disease Diagnosis and Prognosis

Dinu Rajapakse, Iman Beheshti, Ji Hyun Ko
Rady Faculty of Health Sciences

INTRODUCTION

Parkinson's Disease (PD) is the second most common neurodegenerative disorder in the world[1]. PD manifests in patients with a variety of motor and cognitive symptoms, which progress to debilitating motor symptoms and mild cognitive impairment (MCI) or dementia[1,2].

The causes of PD are largely unknown. Genetic markers have been associated with PD. Multiple other factors are believed to be involved in the development of PD as well[2]. This gap in knowledge limits the understanding of the development and progression of PD. This has made clinical diagnosis and prognosis of PD unclear in the early stages of the disease[3]. The late diagnosis of PD leaves very little time for interventions to treat or slow the progression of PD[3].

Imaging biomarkers are non-invasive indicators of disease status which can be used to aid diagnosis of PD and track the progression of PD to adapt treatment.

AIM

Identify biomarkers for PD diagnosis and prognosis and develop a machine learning program to classify PD images against healthy control (HC) images using the biomarkers identified.

METHOD

○ Collect and organize longitudinal imaging and clinical data of a cohort of PD patients and Healthy Control (HC) individuals, as well as other groups of interest such as SWEDD (scans without dopaminergic deficit) or prodromal

    ○ Data for this research was collected from the Parkinson's Progression Markers Initiative (PPMI) website

○ Preprocess all images according to the same protocol for comparison of images

○ Conduct statistical analysis of images to find correlations between changing imaging characteristics and changing motor, cognitive, and other clinical symptoms in PD

○ Create machine learning program to classify PD vs. HC using selected characteristics

Figure 1. Methodology of determining brain imaging biomarkers. MRI scan on the top left shows the anatomy of the brain, image from [3]. DAT SPECT scans in bottom right show the differences between abnormal and normal striatal binding of dopamine transporter markers, image from [3].

CURRENT FINDINGS

Current studies for PD Imaging biomarkers have focused on DAT-SPECT imaging as a promising biomarker for Parkinson's Disease[3]

- Both qualitative and quantitative measures of DAT imaging have been used to aid Parkinson Disease diagnosis[3]

  - Qualitative examination of DAT-SPECT imaging has been used to improve confidence in PD diagnoses[3]

  - For quantitative methods, Striatal Binding Ratios (SBR) have been shown to be promising indicators of Parkinson's disease[4]

Intracortical diffusivity changes have been identified as another potential biomarker using diffusion tensor imaging (DTI) and structural magnetic resonance imaging (MRI)[1]

FURTHER STUDY

More studies need to be done to confirm the reliability of brain imaging biomarkers for PD across larger, more diverse cohorts.

Further studies should be done to explore the uses of multiple imaging modalities, biological samples, and clinical testing in determining a comprehensive method for diagnosis of PD and tracking disease progression.

Once PD imaging biomarkers have been confirmed, treatments can be developed for slowing the development of PD by treating the biological processes involved, as an alternative to current treatments which aim to alleviate motor symptoms.

APPLICATIONS

Brain imaging biomarkers for PD can be used to understand the mechanisms involved in the development and progression of PD

Brain imaging biomarkers for PD may be able to provide PD diagnosis or prediction of PD onset before distinguishing motor symptoms are present, allowing for the possibility of early intervention and treatment of PD[3]
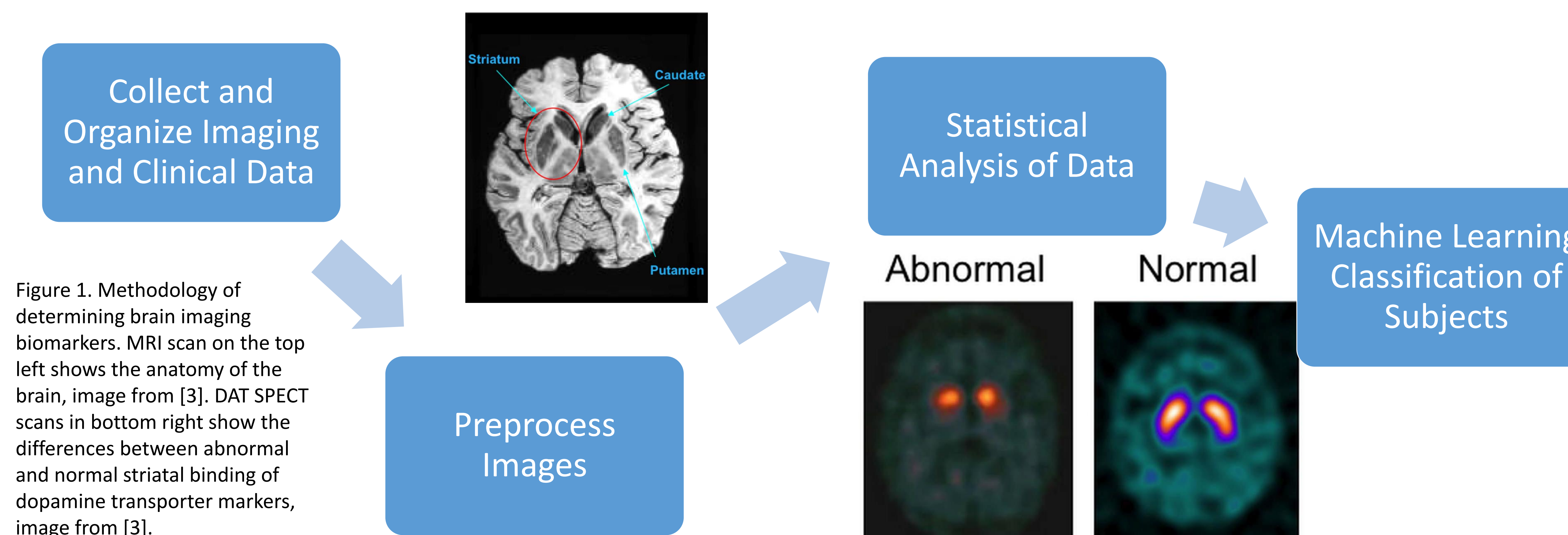
Brain imaging biomarkers allow for a non-invasive method to determine effectiveness of treatments for PD in patients and clinical trials[1]

NOTE ON IMAGING TECHNIQUES

DAT-SPECT Imaging: Dopamine Transporter Single Photon Emission Computerized Tomography. This imaging technique uses a radioactive tracer which binds to dopamine transporter proteins in neurons and indicates the presence or absence of dopamine transporters in the striatal area of the brain[3].

DTI: Diffusion Tensor Imaging. This imaging technique uses the diffusion of water through brain tissues to provide information about the make up of the brain[1].

MRI: Magnetic Resonance Imaging. This imaging technique depicts the organ structure using magnetic fields and radio waves[1].

REFERENCES

[1] Sampedro, F., Martínez-Horta, S., Marín-Lahoz, J., Pagonabarraga, J., & Kulisevsky, J. (2019). Longitudinal intracortical diffusivity changes in de-novo Parkinson's disease: A promising imaging biomarker. Parkinsonism and Related Disorders, 68(September), 22–25. https://doi.org/10.1016/j.parkreldis.2019.09.031

[2] Fahn S. Description of Parkinson's disease as a clinical syndrome. Ann N Y Acad Sci. 2003 Jun;991:1-14. doi: 10.1111/j.1749-6632.2003.tb07458.x. PMID: 12846969.

[3] Bajaj, N., Hauser, R. A., & Grachev, I. D. (2013). Clinical utility of dopamine transporter single photon emission CT (DaT-SPECT) with (123I) ioflupane in diagnosis of parkinsonian syndromes. Journal of Neurology, Neurosurgery and Psychiatry, 84(11), 1288–1295. https://doi.org/10.1136/jnnp-2012-304436

[4] Bayram, E., Kaplan, N., Shan, G., & Caldwell, J. Z. K. (2020). The longitudinal associations between cognition, mood and striatal dopaminergic binding in Parkinson's Disease. Aging, Neuropsychology, and Cognition, 27(4), 581–594. https://doi.org/10.1080/13825585.2019.1653445