ISSN: 2641-1911
DOI: 10.33552/ANN.2022.13.000811
Archives in Neurology & Neuroscience
Iris Publishers

Review Article

Computer Guided Mapping and Treatment of Parkinson's Disease

Kenneth D Eichenbaum[1], Ahmed Fadiel[2]*, Fatemeh Fathabadi[3] and Adam Koster[4]

[1]*Department of Anesthesiology, Oakland University, William Beaumont School of Medicine, USA*

[2]*Computational Oncology Unit, University of Chicago Comprehensive Cancer Center, USA*

[3]*Western Michigan University, 903 W Michigan Ave, Kalamazoo, USA*

[4]*Iris Biologics, 4717 Campus Dr Ste S117, Kalamazoo, Michigan, USA*

Corresponding author: Ahmed Fadiel, University of Chicago. 900 E 57th Street, KCBD Bldg., STE 4144, Chicago, IL 60637, USA.

Received Date: October 22,2022

Published Date: November 14, 2022

Abstracts

Parkinson's disease is a movement disorder often arising from the breakdown and death of dopaminergic neurons in the brain. This results in the catastrophic loss of motor function. The diagnosis of this disease is primarily made through history, symptoms and the outward progressive failure of the motor strip. To better understand the pathobiology of this disease, machine learning algorithms in conjunction with deep learning algorithms that rely on pathophysiological signals, neuroimaging and specific diagnostic tests can be studied and refined to study how interventional techniques and clinical trials can be evaluated. While traditional treatment paradigms have primarily relied on Dopamine supplementation therapy along with disease modifying medications, many of these have demonstrated limited success to date. We discuss strategies and a novel approach aimed at mapping disease progression using an artificial intelligence approach.

Introduction

Parkinson's Disease (PD) is the pathological process involving neurodegeneration and death of the brain cells responsible for trafficking the neurotransmitter dopamine. The hallmark symptoms of Parkinson's Disease are resting tremor, bradykinesia and rigidity In addition to motor symptoms, this disease results in profound autonomic and psychological dysfunction. Additional functional deficits include speech, sleep, eating and swallowing and it is associated with organ-specific and total-body pain [1,2].

What we call PD may be a spectrum of neurologic disease and the usage of artificial intelligence and machine learning can help subdivide the diagnosis to help arrive at the specific pathways involved in this pathologic degradative process.

Precision Medicine and Parkinson's Disease

Diagnosing early PD can be challenging. PD researchers have recently begun work on new computational approaches and algorithms have been initiated to help analyze personalized profiles of neuronal degeneration and its clinical presentation. The current definitions of precision medicine are imprecise but mainly refer to usage of computational methods to better decide treatment strategies based on the individual characteristics of each patient. As such precision medicine guided by machine learning of this disease can individualize new prevention and treatment strategies according to each patient's specific pathology. By isolating the individual traits and generating a machine-assisted comprehensive

patient map in each individual patient, it may be easier to select which therapeutic intervention may have the most chance for success.

Perhaps this approach will facilitate fewer off-target therapies and improve the targeted patient population for PD treatments.

Machine Learning in Parkinson's Disease

The first effort to characterize PD in a more rigorous data collection approach was the Parkinson's Progression Markers Initiative (PPMI). Developed in 2010, this study was a longitudinal observational study, following 1500 participants, using clinical and imaging data and biological samples from 33 clinical sites around the world [3].

Building on that dataset and more recent biomarker data, algorithms can be developed using functional inputs for detecting progression of PD. Data inputs can be broken down into Pathophysiological signals, Neuroimaging Techniques and a collection of miscellaneous modalities (Figure 1).

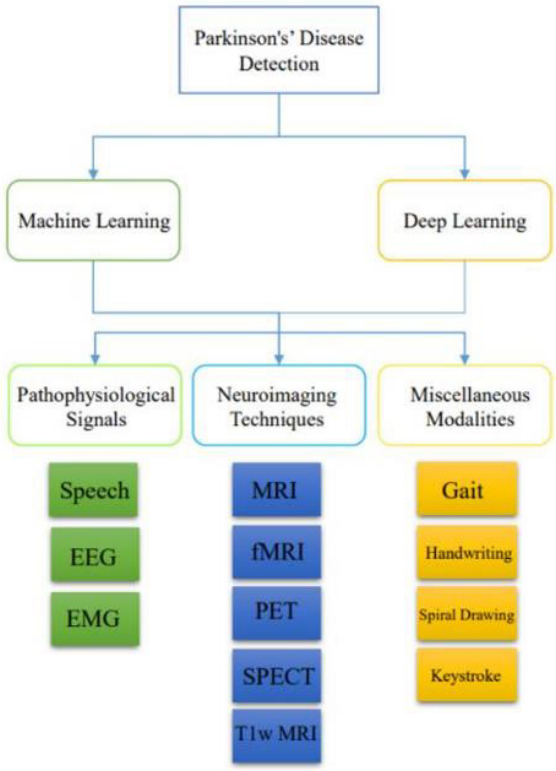

Figure 1: Diagnostic Inputs for Parkinson's Disease.

Key pathophysiological diagnostic inputs include speech, electroencephalography and electromyography. Neuroimaging Techniques include MRI, fMRI, PET scan, SPECT scan and T1 weighted MRI. Evaluating neuroimaging with machine learning has employed feature extraction and selection methods such as principal and independent component analysis, linear modeling and wrapper selection methods with internal selection filters. The known classifiers are scored with accuracy and include LS-SVM, Multi Kernel SVM, GLM, Boosted, LR, LDA, and PBL-McRBFN. To date, SVM has demonstrated best results [4-8]. Other modalities for evaluation of PD involve gait, writing and drawing samples and keystroke datasets. Similar classifier techniques have been used to organize these datasets including k-nearest neighbors, SVM, ensemble and adaptive boosting [9,10].

Moving from Current Treatment Modes to Future Treatment Modes

Dopamine has been used as a treatment for the spectrum of PD. While dopamine is unable to cross the blood brain barrier, its precursor, L-Dopa, can and is readily converted to dopamine in the brain [11]. L-Dopa therapies continue to be used in PD treatment, however this mode of therapy fails as the disease progresses. With poor available therapies, treatment of Parkinson's Disease (PD) has been subdivided into 1. symptomatic therapy with symptom reduction using both dopamine and alternative medications, and 2. developing new disease modifying treatments, using pathway- and receptor-targeted medications. McFarthing et al. recently characterized the major treatment categories associated with both symptomatic therapy and disease modifying treatments [12].

An individualized medicine approach can focus on improving disease modifying treatments and help map the pathologic presentation into a more granular pathology and isolate the specific disease modifiers that will have the best chance for success. For example, can specific disease traits be mapped to correlate with inflammatory and infectious etiologies, with oxidative stress, or with the formation of α-synuclein?

Current trials for PD therapies target inflammatory and infectious etiologies which may act to degrade brain cell function prior to identifiable pathology and the onset of motor symptoms. The specific involvement of dopamine immunogenicity is poorly understood, although there is known involvement at synapses where dendrites interact with lymphocytes and in germinal centers with B- and T- cells [13,14].

Along with the decline in neuronal dopamine, Lewy bodies with known α-synuclein protein aggregates in the substantia nigra, are a central pathological finding in PD brain cells. Their role in impairing axonal and synapse functions remains unclear [15,16] Phosphorylated α-synuclein has been identified in the enteric nervous system and retrograde gut to brain translocation mechanisms are potentially implicated [17,18]. Deep learning can improve forecasting of which therapies will improve these pathological branch points.

More recently newer biomarkers for inflammation and neurodegenerative pathologies are gaining increased attention in the PD community and can be harnessed for deep learning. In particular, Neurofilament light (NfL), a marker of axonal nerve degeneration, has shown promise as a marker of severity and progression of PD and may be an excellent measure of clinical disease course [19].

Next Steps for Intelligent Mapping of PD

We aim to generate an array of subtypes of PD. To accomplish this aim, a parallel deep fusion framework is in development for diagnosis of specific Parkinson's Disease subtypes. This approach will harness innovative fusion strategies along with Deep Neural Network Architectures to combine clinical, imaging, biological, and genetic data.

We suggest using the PPMI dataset and the numerical, categorical, and image data a Parallel Deep Fusion Framework is proposed for developing a PD subtype diagnosis. In this approach, innovative fusion strategies along with Deep Neural Network architecture will be used to combine clinical, imaging, biological, and genetic data. Our proposed method consists of three parallel paths based on the result of any deep or machine learning algorithms that have high accuracy. The three parallel paths are followed by a multilayer fusion layer, acting as a fusion center that combines localized features.

A machine/deep learning dataset is defined as the collection of data, training the model and predicting results. For many medical imaging analysis applications, a deep Convolutional Neural Network (CNN) is applied to perform segmentation tasks of MRI.

In the segmentation method, the reference standard, which is the target region of interest, based on different subtypes of PD, is defined by manual annotation of all scans in 2-D slices. In contrast, with machine/deep learning models, all input and output variables must be numeric. So the categorical data can be encoded into numbers prior to fitting and evaluating the model. Also, numerous strategies will be applied for transforming raw numerical data into features purpose-built for machine/deep learning algorithms in order to find the most accurate model. Finally, the fused data can be applied to a multi-input parallel deep fusion model to be trained. Refining the dataset provides a more precise methodology based on the specifications of each sample and feature.

Conclusion

Machine learning-assisted diagnosis of PD can vastly improve the clinical management of this disease. Incorporating novel biomarkers will improve PD diagnosis at an earlier stage. This will involve creating larger datasets and diagnostic information from which to draw. To diagnose and establish subtypes of PD, a parallel deep fusion framework for Parkinson's Disease subtypes diagnosis can be developed. In this approach, innovative fusion strategies along with Deep Neural Network Architectures is in development to combine clinical, imaging, biological, and genetic data.

Acknowledgement

None.

Conflict of Interest

No financial interest or conflict of interest exists.

Contributors

All authors contributed to the authorship and preparation of this manuscript.

References

1. E Gökçal, GÜR Veysel Eren, R Selvitop, GB Yildiz, A Talip (2017) Motor and non-motor symptoms in Parkinson's disease: effects on quality of life. Arch Neuropsychiatry 54(2): 143.
2. Kara J Wyant (2017) Motor and Non-Motor Symptoms for Diagnosing Parkinson's Disease," Michigan Medicine, University of Michiga.
3. (2010) "Parkinson's Progression Markers Initiative (PPMI)". https://www.michaeljfox.org/news/parkinsons-progression-markers-initiative-ppmi
4. Z Soumaya, BD Taoufiq, N Benayad, K Yunus, A Abdelkrim (2021) The detection of Parkinson disease using the genetic algorithm and SVM classifier. Appl Acoust 171: 107528.
5. L Ali, C Zhu, Z Zhang, Y Liu (2019) Automated detection of Parkinson's disease based on multiple types of sustained phonations using linear discriminant analysis and genetically optimized neural network," IEEE J. Transl Eng Heal Med 7: 1-10.
6. CO Sakar et al., (2019) A comparative analysis of speech signal processing algorithms for Parkinson's disease classification and the use of the tunable Q-factor wavelet transform. Appl Soft Comput 74: 255-263.
7. P Sharma, S Sundaram, M Sharma, A Sharma, D Gupta (2019) Diagnosis of Parkinson's disease using modified grey wolf optimization. Cogn Syst Res 54: 100-115.
8. E Benmalek, J Elmhamdi, A Jilbab (2017) Multiclass classification of Parkinson's disease using different classifiers and LLBFS feature selection algorithm. Int J Speech Technol 20(1): 179-184.
9. S Saravanan, Kannan Ramkumar, K Adalarasu, Venkatesh Sivanandam, S Rakesh Kumar, et al. (2022) A Systematic Review of Artificial Intelligence

(AI) Based Approaches for the Diagnosis of Parkinson's Disease. Arch Comput. Methods Eng: 1-15.

10. KR Bhatele, SS Bhadauria (2020) Brain structural disorders detection and classification approaches: a review. Artif Intell Rev 53(5): 3349-3401.

11. Franco R, Reyes-Resina I, Navarro G (2021) Dopamine in Health and Disease: Much More Than a Neurotransmitter. Biomedicines 9(2): 109.

12. McFarthing K, Rafaloff G, Baptista M, Mursaleen L, Fuest R, et al. (2022) Parkinson's Disease Drug Therapies in the Clinical Trial Pipeline: 2022 Update. J Parkinsons Dis 12(4):1073-1082.

13. Papa I, Saliba D, Ponzoni M, Bustamante S, Canete PF, et al. (2017) TFH-derived dopamine accelerates productive synapses in germinal centres. Nature 547: 318-323.

14. Franco R, Reyes-Resina I, Navarro G (2021) Dopamine in Health and Disease: Much More Than a Neurotransmitter. Biomedicines 9(2): 109.

15. Lin KJ, Lin KL, Chen SD, Liou CW, Chuang YC, et al. (2019) The Overcrowded Crossroads: Mitochondria, Alpha-Synuclein, and the Endo-Lysosomal System Interaction in Parkinson's Disease. Int J Mol Sci 20(21): 5312.

16. Stefanis L (2012) α-Synuclein in Parkinson's disease. Cold Spring Harb Perspect Med 2(2): a009399.

17. Nielsen SD, Pearson NM, Seidler K (2021) The link between the gut microbiota and Parkinson's Disease: A systematic mechanism review with focus on α-synuclein transport. Brain Res 1769: 147609.

18. Keshavarzian A, Engen P, Bonvegna S, Cilia R (2020) The gut microbiome in Parkinson's disease: A culprit or a bystander? Prog Brain Res 252: 357-450.

19. Chin-Hsien Lin, Cheng-Hsuan Li, Kai-Chien Yang, Fang-Ju Lin, Chau-Chung Wu, et al. (2019) Blood NfL A biomarker for disease severity and progression in Parkinson disease. Neurology 93(11): e1104-e1111.