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Unraveling the characteristics of Parkinson's Disease through neuroimaging: Insights and future directions

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Abstract. Parkinson's disease (PD) is a neurodegenerative disease with a high degree of patient heterogeneity, and as of 2016 there are approximately 6.1 million PD patients worldwide. PD has a high proportion of patients with intermediate to advanced disease and a high rate of disability, and clinical diagnosis and treatment are difficult due to the lack of neuromarkers to identify disease states and the inability to quantify the effects of treatment in PD. In recent years, many researchers have explored specific changes in brain activity in PD based on electrophysiological and neuroimaging data. Electroencephalography, with its high temporal resolution and rich frequency domain information, and functional magnetic resonance imaging, with its high spatial resolution, have become the main tools to characterize the state of brain activity in PD in recent years. This paper analyses some of the available data on the characteristics of PD through two neuroimaging techniques commonly used in the disease. It concludes with the prospect of being able to establish uniform criteria for determining PD.

Keywords: EEG, functional MRI, neural characteristics, brain activity, Parkinson's disease.

1. Introduction

Parkinson's disease (PD) is a neurodegenerative disease with common symptoms such as static tremor, rigidity, bradykinesia, postural gait disturbances, and non-motor symptoms including cognitive impairment and insomnia [1].

By 2016, there were about 6.1 million PD patients all over the world, and over 1.41 million PD sufferers in China[2]. With the further aging of China, some scholars speculate that China's PD patient population may reach to close to 5 million by 2030, accounting for 57% of the PD patients[3]. The high proportion of middle and late stage PD patients with leads to a high disability rate of the disease, and the treatment is expensive and irreversible, requiring long-term care of patients and physicians, thus PD places a heavy burden on families and society[4].

In recent years, there has been rapid development in neuroimaging techniques, providing effective means to decipher the specific brain activity patterns associated with PD[5]. Advanced clinical methods for detecting brain activity have paved the way for understanding the distinctive neural characteristics of PD. Currently, commonly used techniques for detection include EEG, functional magnetic resonance imaging (fMRI) and so on.

Electroencephalography (EEG) is a technique used to record highly time-resolved brain electrical signals. It measures the voltage difference between recording electrodes and reference electrodes, and

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the voltage changes over time form the waveform of the EEG[6]. EEG provides valuable information for clinical diagnosis of various psychiatric disorders such as epilepsy[7] and sleep disorders[8].

The fMRI signal comes directly from the neural activity of the brain; it is noninvasive, applicable to subjects of all ages, and the same subject can participate in the experiment several times within a short period of time; the spatial resolution is very high, which allows for precise functional localization; and it provides a wide range of parameters, which can meet the various requirements of the experimenter.

Additionally, PD patients' motor symptoms can be effectively treated by deep brain stimulation (DBS). A surgical technique known as DBS is carried out in neurosurgery and entails implanting a device known as a neurostimulator. This device delivers electrical pulses through implanted electrodes to specific targets (brain nuclei) in the brain. DBS is used to treat PD, essential tremor, dystonia, and other movement disorders caused by conditions[9] such as obsessive-compulsive disorder and epilepsy.

Although the exact underlying principles and mechanisms of DBS are not yet fully understood, it is a controlled method to directly modulate brain activity. Deciphering the regulatory mechanisms of DBS on PD is essential for quantifying the therapeutic effects of DBS and predicting its efficacy[10, 11]. It holds great significance and value in providing clinically effective treatment for patients with PD.

2. EEG-based characteristics of brain activity in Parkinson's disease

Brain rhythms are grouped into different frequency bands according to the logarithmic increase in central frequency and bandwidth. The frequency bands of brain rhythms include: δ (0–4 Hz), θ (5–7 Hz), α (8–13 Hz), β (14–30 Hz), and γ (>30 Hz). In addition, there are other frequency bands of rhythms, but this article primarily uses the above-mentioned bands for analysis. Research has shown that in PD patients, the relative increase in theta and delta band activities is observed, while alpha and beta band activities are relatively decreased compared to healthy control groups[12]. Further studies have also demonstrated that the frequency characteristics in the EEG of PD patients vary with different clinical phenomena. Compared to non-dementia PD patients, patients with dementia associated with PD exhibit increased amplitude in the delta and theta bands, and decreased amplitude in the alpha and beta bands. Abnormal cortical theta rhythm is observed in the posterior region based on cortical source mapping of resting-state EEG. Patients with mild cognitive impairment in Parkinson's disease (PD-MCI) exhibit higher relative power in the theta band compared to cognitively normal Parkinson's disease patients (PD-CogN1). From PD-CogN1 to PD-MCI and then to Parkinson's disease dementia (PDD), there is an upward trend in delta band power[13]. For PD patients with mild to moderate motor impairments, longitudinal changes in neuropsychological tests are mainly associated with changes in delta power[14, 15]. Compared to the healthy control group, PD patients have higher diffuse delta sources, which may contribute to the abnormal central delta rhythm in PD. This may lead to abnormal central delta rhythm sources in PDD patients. The increase in delta band power may be a primary feature of cognitive impairment worsening, which is closely associated with the incidence of PDD[16].

EEG microstates are spatial patterns that show stability within a specific time window. Each microstate represents a particular pattern of brain activity and lasts from tens to hundreds of milliseconds[17]. It has been found that different EEG microstates are associated with specific cognitive processes and functional brain networks. Thus, by analyzing EEG microstates, we can reveal the functional connectivity and regulation of the brain under different tasks, states, and diseases, thereby improving our understanding of brain function. The brain topography can be classified in several ways, among which Michel C. M et al. There are four EEG microstates: A, B, C, and D[17]. The superior and middle temporal lobes were found to be negatively activated by BOLD in microstate A, whereas the occipital cortex was found to be negatively activated by BOLD in microstate B. Additionally, microstate C was linked to positively activated BOLD in the dorsal anterior cingulate cortex, inferior frontal cortex, and right insular area, while microstate D was linked to negatively activated BOLD in the dorsal anterior cingulate cortex, inferior frontal cortex, and right insular area.Certain clinical symptoms are brought on by cognitive tiredness, which is linked to an increased mean duration of microstate B. Microstate B was seen in PD patients at considerably greater frequencies and with mean durations that progressively reverted to normal when cognitive ability increased[18]. In PD patients, there is an increase in the

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average duration and frequency of microstate A; a decrease in the average duration and frequency of microstate C; and an increase in the average duration, frequency, and coverage of microstate D[19].

Deep Learning (DL) algorithms have recently achieved great success in many domains involving images, text, video and speech, and this approach has greatly improved the accuracy of data recognition and allowed the discovery of complex structural features in complex high-dimensional data[20]. Khojasteh et al used a deep convolutional neural network to classify the spectral features of the pronunciations of PD patients and healthy individuals, showing that speech recognition combined with deep learning can help to screen PD patients[21]. In order to predict PD, Zhang RL et al. coupled time-domain analysis with deep learning and used the deep residual shrinkage network wavelet packet transform and the deep residual shrinkage network adjustable Q-factor wavelet transform. PD for prediction and its accuracy was brought to 92.3%[22]. The above study shows that DL is an algorithm with great potential, which has already achieved excellent results in multi-domain analysis using EEG signals as input.

3. MRI-based characteristics of brain activity in Parkinson's disease

fMRI is a method in magnetic resonance imaging that tracks changes in blood oxygen levels in brain regions through blood oxygen level-dependent imaging (BOLD), enabling non-invasive observation of brain activity. fMRI has been widely used in the study and diagnosis of a variety of brain disorders[23]. This part will analyze in terms of voxels, regions of interest and brain networks.

3.1. Voxel-based analysis

The fMRI captures multiple 2D images in a short period of time through a scanning device and then combines these 2D images to form a 3D image of the entire brain (Volume). In addition to resting-state brain functional connectivity and large-scale analyses, regional homogeneity (ReHo) has been an important method for detecting local neural synchrony, which uses regional BOLD signals to measure similarity in time series within brain-wide regions. It has been effective in identifying local neuronal synchrony in both neurodegenerative illnesses and healthy aging people[24]. Comparisons between cognitively normal Parkinson's disease patients (PD-CN) and normal controls (NC) showed that the DMN, sensorimotor network, basal ganglia, left angular gyrus and left anterior central gyrus showed increased ReHo changes[25-28]. Whereas, ReHo alterations were decreased in frontal, occipital, primary sensory cortex, visual network and cerebellar regions[27-30]. Abnormal ReHo indices are seen in the DMN in Parkinsonian subtypes without cognitive impairment, such as tremor-dominant and postural instability difficulty-dominant Parkinson's disease individuals[26, 27, 31, 32]. In addition to cross-sectional studies, a longitudinal study of PD patients in normal conditions over a period of two years showed a decrease in ReHo index in the DMN over time[29]. We can offer helpful information for the early diagnosis of Parkinson's syndrome through the changes in ReHo by analyzing the aforementioned research. Li-Chuan Huang et al[33] defined and measured brain regions by VBM, which showed the distribution of significant clusters of brain atrophy in patients with PD compared to Healthy control (HC) (with a cluster threshold of p-uncorrected <0.001) in the Distribution. Brain regions that were significantly reduced in PD patients compared to HC participants included the left temporal lobe, left middle temporal lobe, middle temporal gyrus, white matter, parietal lobe, and posterior central gyrus. In addition, using low-frequency fluctuation amplitude and ReHo as an index of resting-state fMRI, the investigators found that PD patients with MCI had abnormal resting brain activity in the left middle temporal gyrus, right superior temporal gyrus, left superior frontal gyrus, right inferior frontal gyrus[28, 34], left insula, and left precuneus[35]. In comparison to PD patients without MCI, the "structural atrophy" and "abnormal functional activity" may point to neural plasticity (or synaptic loss), hyperexcitability, and modifications to neuronal networks.

3.2. Regions of interest based analysis

Brain regions of interest are areas that are commonly associated with a function, cognitive process, or disease state in neuroscience research or clinical applications. Symptoms of dyskinesia in PD patients

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are thought to be the result of deficits in motor circuits, including the supplementary motor area, part of the premotor cortex, and the primary motor cortex[30], and these studies have demonstrated evidence of reduced cerebral blood flow in the SMA[36-38], prefrontal and cingulate cortexes[38, 39], and in M1[36]. Moreover, relative to HC, primary motor cortex and supplementary motor areas are underactivated in PD patients[40].Marta Moraschi et al[41], by comparing PD patients with healthy volunteers performing a task with the hand, observed that the cingulate cortex and dorsolateral prefrontal cortex in PD patients were consistently activated during the performance of the task with the affected hand and that, relative to the healthy hemisphere, the patients had reduced blood flow to the cingulate and prefrontal cortex in the affected hemisphere[36, 42], motor cortex in the affected hemisphere showed greater and stronger activation. In contrast to controls, patients had hyperactivation in the damaged hemisphere's dorsolateral prefrontal cortex. Rimona S. Well et al[42] found that performance on this task was related to activity in the posterior cingulate cortex/precuneus by visually comparing the differences between patients who performed well and those who performed poorly on a perceptual task.

3.3. Brain-networks based analysis

Brain networks are organized structures in the brain where different regions connect and interact with each other. These regions form complex networks through synaptic connections between neurons and play important roles in information processing, cognitive functions and behavior. Over the past two decades, a large number of scholars have extensively studied brain functional connectivity using resting-state functional magnetic resonance imaging[43-47], which is an efficient and convenient method for analyzing brain networks. Studies have demonstrated disturbances in the functional integration of network connectivity in patients with PD[48-53], significant decreases in nodal and global efficiency[48], reduced effectiveness of information transfer within the motor cortex-basal ganglia pathway[51], reduced functional integration between neural networks involving the striatum, midbrain limbic cortex, and sensory-motor regions[50], as well as from the frontal-occipital junction to motor cortex decreased connectivity[53]. Using resting-state fMRI, some researchers have discovered that functional disconnections may be linked to MCI in PD. For instance, it was shown that PD patients with MCI had disrupted connectivity in the DMN, which is closely linked with cognitive functions[54]. Nevertheless, a different research revealed that PD patients, independent of their cognitive state, had altered functional connectivity of the DMN, whereas PD-MCI was linked to functional disconnection of the frontal network but no structural alterations were seen.[55]. Furthermore, research on dynamic functional connectivity points to a dynamic decline in brain function in PD-MCI patients that is absent in PD patients without MCI. These data imply that disruption of functional connectivity or functional networks, in addition to abnormalities in distinct brain regions, may be involved in the neural mechanisms of PD-MCI.

4. Conclusion

In this paper, we discuss some characteristic indicators of PD patients from both EEG and functional MRI. Through EEG analysis, we can see that PD patients have increased activity in the theta and delta bands and decreased activity in the α and β bands; PD patients with concomitant cognitive impairment show higher amplitudes in the delta and theta bands, and decreased amplitudes in the α and β bands. Changes in EEG microstates and the application of deep learning algorithms show the potential to understand the brain functions related to PD, and to aid in the detection and prediction of PD. Findings based on fMRI studies include atrophy of brain regions, reduced blood flow and disorders of brain functional connectivity with reduced nodal and global efficiency, and these abnormalities may be associated with motor impairment and cognitive decline. From the above analysis, we can know that there are many indicators and means of analysis to discriminate PD, and the response is different through different means of analysis. On top of that, due to the heterogeneity of PD patients, it is difficult to find consistency in the results determined by the same methods. Therefore, we need a unified standard to judge PD afterwards.

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References

[1] Kalia, L.V. and A.E.J.T.L. Lang, Parkinson's disease. 2015. 386(9996): p. 896-912.
[2] Dorsey, E.R., et al., Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. 2018. 17(11): p. 939-953.
[3] Chaudhuri, K.R., et al., The Cost Effectiveness of Levodopa-Carbidopa Intestinal Gel in the Treatment of Advanced Parkinson's Disease in England. 2022. 40(5): p. 559-574.
[4] Zhang, Y., et al., Neuroimaging in Parkinson's disease and Parkinsonism. 2023. 14: p. 1153682.
[5] Biasiucci, A., B. Franceschiello, and M.M.J.C.B. Murray, Electroencephalography. 2019. 29(3): p. R80-R85.
[6] Aboalayon, K.A.I., et al., Sleep stage classification using EEG signal analysis: a comprehensive survey and new investigation. 2016. 18(9): p. 272.
[7] Acharya, U.R., et al., Automated EEG analysis of epilepsy: a review. 2013. 45: p. 147-165.
[8] Kringelbach, M.L., et al., Translational principles of deep brain stimulation. 2007. 8(8): p. 623-635.
[9] Hammond, C., et al., Latest view on the mechanism of action of deep brain stimulation. 2008. 23(15): p. 2111-2121.
[10] García, M.R., et al., A slow axon antidromic blockade hypothesis for tremor reduction via deep brain stimulation. 2013. 8(9): p. e73456.
[11] Han, C.-X., et al., Investigation of EEG abnormalities in the early stage of Parkinson's disease. 2013. 7: p. 351-359.
[12] Caviness, J., et al., Differential spectral quantitative electroencephalography patterns between control and Parkinson's disease cohorts. 2016. 23(2): p. 387-392.
[13] Babiloni, C., et al., Cortical sources of resting state electroencephalographic rhythms in Parkinson's disease related dementia and Alzheimer's disease. 2011. 122(12): p. 2355-2364.
[14] Babiloni, C., et al., Levodopa may affect cortical excitability in Parkinson's disease patients with cognitive deficits as revealed by reduced activity of cortical sources of resting state electroencephalographic rhythms. 2019. 73: p. 9-20.
[15] Caviness, J.N., et al., Longitudinal EEG changes correlate with cognitive measure deterioration in Parkinson's disease. 2015. 5(1): p. 117-124.
[16] Lehmann, D., et al., EEG alpha map series: brain micro-states by space-oriented adaptive segmentation. 1987. 67(3): p. 271-288.
[17] Michel, C.M. and T.J.N. Koenig, EEG microstates as a tool for studying the temporal dynamics of whole-brain neuronal networks: a review. 2018. 180: p. 577-593.
[18] Hanoglu, L., et al., Therapeutic role of repetitive transcranial magnetic stimulation in Alzheimer's and Parkinson's Disease: electroencephalography microstate correlates. 2022. 16: p. 798558.
[19] Kim, D. and K. Kim. Detection of early stage Alzheimer's disease using EEG relative power with deep neural network. in 2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). 2018. IEEE.
[20] Khojasteh, P., et al. Parkinson's disease diagnosis based on multivariate deep features of speech signal. in 2018 IEEE Life Sciences Conference (LSC). 2018. IEEE.
[21] Zhang, R., et al., EEG analysis of Parkinson's disease using time–frequency analysis and deep learning. 2022. 78: p. 103883.
[22] Calhoun, V.D., et al., The chronnectome: time-varying connectivity networks as the next frontier in fMRI data discovery. 2014. 84(2): p. 262-274.
[23] Li, J., et al., Alterations in regional homogeneity of resting-state brain activity in fatigue of Parkinson's disease. 2017. 124: p. 1187-1195.
[24] Pan, P.L., et al., Aberrant regional homogeneity in Parkinson's disease: A voxel-wise meta-analysis of resting-state functional magnetic resonance imaging studies. 2017.
[25] Guo, W., et al., Brain activity alterations in patients with Parkinson's disease with cognitive impairment based on resting-state functional MRI. 2021. 747: p. 135672.

DOI: 10.54254/2755-2721/57/20241313

[26] Harrington, D.L., et al., Aberrant intrinsic activity and connectivity in cognitively normal Parkinson's disease. 2017. 9: p. 197.
[27] Choe, I.-H., et al., Decreased and increased cerebral regional homogeneity in early Parkinson's disease. 2013. 1527: p. 230-237.
[28] Li, M.-g., et al., Alterations of regional homogeneity in Parkinson's disease with mild cognitive impairment: a preliminary resting-state fMRI study. 2020. 62: p. 327-334.
[29] Ge, A.J.P.B.R., Basal ganglia-thalamocortical circuite: Parallel substrates for motor, oculomotor," prefrontal" and" limbic" functions. 1990. 85: p. 119-146.
[30] Huang, L.-C., et al., Graph theory and network topological metrics may be the potential biomarker in Parkinson's disease. 2019. 68: p. 235-242.
[31] Li, Y., et al., Abnormal regional homogeneity in Parkinson's disease: a resting state fMRI study. 2016. 71(1): p. e28-e34.
[32] Zeng, Q., et al., Longitudinal alterations of local spontaneous brain activity in Parkinson's disease. 2017. 33: p. 501-509.
[33] Gao, L., et al., Brain activity in Parkinson's disease patients with mild cognitive impairment. 2016. 61: p. 1876-1883.
[34] Wang, Z., et al., Abnormal spontaneous brain activity in early Parkinson's disease with mild cognitive impairment: a resting-state fMRI study. 2018. 9: p. 1093.
[35] Moraschi, M., et al., fMRI study of motor cortex activity modulation in early Parkinson's disease. 2010. 28(8): p. 1152-1158.
[36] Rascol, O., et al., Normal activation of the supplementary motor area in patients with Parkinson's disease undergoing long-term treatment with levodopa. 1994. 57(5): p. 567-571.
[37] Playford, E.D., et al., Impaired mesial frontal and putamen activation in Parkinson's disease: a positron emission tomography study. 1992. 32(2): p. 151-161.
[38] Hsu, J.-L., et al., Regional CBF changes in Parkinson's disease: a correlation with motor dysfunction. 2007. 34: p. 1458-1466.
[39] Buhmann, C., et al., Pharmacologically modulated fMRI---cortical responsiveness to levodopa in drug‐naive hemiparkinsonian patients. 2003. 126(2): p. 451-461.
[40] Greicius, M.J.C.o.i.n., Resting-state functional connectivity in neuropsychiatric disorders. 2008. 21(4): p. 424-430.
[41] Weil, R.S., et al., Neural correlates of early cognitive dysfunction in Parkinson's disease. 2019. 6(5): p. 902-912.
[42] During, R.C.B.F.C.J.A.N., Supplementary and Primary Sensory Motor Area Activity in Parkinson's Disease. 1992. 49: p. 144-148.
[43] Li, J., et al., Global signal regression strengthens association between resting-state functional connectivity and behavior. 2019. 196: p. 126-141.
[44] Nostro, A.D., et al., Predicting personality from network-based resting-state functional connectivity. 2018. 223: p. 2699-2719.
[45] Lee, M.H., C.D. Smyser, and J.S.J.A.J.o.n. Shimony, Resting-state fMRI: a review of methods and clinical applications. 2013. 34(10): p. 1866-1872.
[46] Zalesky, A., et al., Time-resolved resting-state brain networks. 2014. 111(28): p. 10341-10346.
[47] Skidmore, F., et al., Connectivity brain networks based on wavelet correlation analysis in Parkinson fMRI data. 2011. 499(1): p. 47-51.
[48] Skidmore, F., et al., Reliability analysis of the resting state can sensitively and specifically identify the presence of Parkinson disease. 2013. 75: p. 249-261.
[49] Luo, C., et al., Reduced functional connectivity in early-stage drug-naive Parkinson's disease: a resting-state fMRI study. 2014. 35(2): p. 431-441.
[50] Wei, L., et al., Reduced topological efficiency in cortical-basal ganglia motor network of Parkinson's disease: a resting state fMRI study. 2014. 9(10): p. e108124.
[51] Suo, X., et al., Functional brain connectome and its relation to Hoehn and Yahr stage in Parkinson disease. 2017. 285(3): p. 904-913.

DOI: 10.54254/2755-2721/57/20241313

[52] Thibes, R.B., et al., Altered functional connectivity between precuneus and motor systems in Parkinson's disease patients. 2017. 7(10): p. 643-647.
[53] Hou, Y., et al., Dysfunction of the default mode network in drug-naive parkinson's disease with mild cognitive impairments: a resting-state fMRI study. 2016. 8: p. 247.
[54] Amboni, M., et al., Resting-state functional connectivity associated with mild cognitive impairment in Parkinson's disease. 2015. 262: p. 425-434.
[55] Díez-Cirarda, M., et al., Dynamic functional connectivity in Parkinson's disease patients with mild cognitive impairment and normal cognition. 2018. 17: p. 847-855.