Detection methods of Parkinson's Disease based on physiological signals and machine learning methods

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Abstract. Parkinson's disease (PD) is an extremely complex motor disorder due to the lack of dopaminergic neurons in the substantia nigra. and other dopaminergic and non-dopaminergic regions of the brain. The high rate of misdiagnosis in Parkinson's disease often causes patients to miss out on the best treatment opportunities. Since some of the symptoms of Parkinson's disease are mild in the initial stages and become severe over time, it is particularly important to correctly diagnose Parkinson's disease timely. The traditional tremor detection method of Parkinson's disease is more complex and the misdiagnosis rate is high. Methods based on physiological signals such as Local field potential (LFP), Electromyographic signal (EMG) and EEG signal et.al and research by using the machine learning strategies including the traditional machine learning and deep leaning methods are increasing. Get a precise diagnosis for Parkinson's disease, this paper analyzes physiological signals and machine learning methods that commonly used in PD detection, which may provide theoretical and practical references to future studies.

Keywords: Parkinson's disease (PD); Physiological signals; machine learning.

1. Introduction

Parkinson's disease is one of the most widespread and devastating neuro-degeneration [1] diseases characterized by motor disorders in the world (WHO, 2006). Parkinson's disease is a chronic and progressive neuropathy due to [2] the absence of dopaminergic neurons in the substantia nigraet other dopaminergic and nondopaminergic regions of the brain. This will lead to motor and nonmotor symptoms such as muscle stiffness, death, hand tremors, voice changes, posture, mood, gait instability, asymmetrical rest, slower movement and more. The clinical manifestations are mainly motor disorders, and its characteristic clinical manifestations are static tremor, myotonia, bradykinesia and postural instability [3]. These symptoms are mild in the initial [1] stages and become severe [1] over time. Over 10 million people have been diagnosed globally, and people with PD have recently been diagnosed as having mental disabilities. It is observed that people around 50 years or older have a higher probability of being diagnosed with PD [4].

Several methods have been frequently used for rapid detection of Parkinson's disease including the subjective assessment (such as UPDRS scales and so on) and objective methods (such as neural image based methods, physiological signals based methods and so on). The clinical commonly used PD assessment scales include Hoehn & Yahr grading scale [5] and standard Parkinson's disease scale (Unified Parkinson's Disease Rating Scale [6], UPDRS), in which a total of 199 points were scored, and higher scores indicate more severe clinical symptoms. Considering about the objective methods, there are few objective and reliable diagnosis and evaluation methods, especially in the early stage (preclinical stage, there is still no effective diagnostic method) Studies have pointed out that 20% of patients diagnosed with Parkinson's disease are actually other diseases, such as essential tremor (ET), enhanced physiological tremor (EPT), multisystem atrophy (MSA), progressive supranuclear nuclear palsy, and cerebrovascular disease. Therefore, it is known that the traditional tremor detection method of PD is complex and has a high misdiagnosis rate [7].Specific tests of other objective methods were performed based on the possible etiology of tremor, such as necessary liver function tests in young patients with non-drug tremor, CSF monoclonal immunoglobulin electrophoresis, head MRI and positron emission tomography, blood flow and metabolism, etc. However, imaging examination still has defects such as complex operation and not suitable for large-scale population detection. Therefore, more and more studies tend to detect signals based on physiological signals include EMG, EEG and LFP.

This study mainly proposes two methods to diagnose Parkinson's disease. Some studies have shown that in the local field potential, the basal ganglia nucleosome produces abnormal neural electrical activity, and Parkinson's tremor shows abnormal oscillation. On the one hand, a large number of studies have shown that in the local field potential, the basal ganglia nucleosome produces abnormal neural electrical activity, and Parkinson's tremor shows abnormal oscillation. Electromyography (EMG) is the motor unit action potential (MUAP) in muscle fibers. Its signal is mainly strengthened with the superposition of time and space. EEG is the synthesis of postsynaptic potential of brain neurons. It is the potential distribution on the scalp after the EEG field is transmitted through the volume conductor [8].EEG reflects the electrical activity of brain tissue and the functional state of brain. Current biomedical signal analysis, including medical imaging, has long been used in feature extraction based applications, combining quantitative and qualitative processing [9].On the other hand, at present, machine learning (ML) and deep neural network (DNN) have been developed rapidly in main signal processing, such as computer vision, speech recognition, human-computer interaction and natural language processing. Through these technologies, we cannot only analyze a large number of data, signals, images and image sequences, but also find the calculation mode, classify, regress and predict the data.

2. Physiological signal

There are several physiological signals that were reported to be used in the diagnosis of PD (including EEG, ECoG, LFP EMG and so on).Among which, the Local field potential (LFP) signals represent the sum of extracellular low-frequency electrophysiological signals in a small number of neural tissue recording electrodes [8]. Electromyography signaling (EMG) is the superposition of motor unit action [10] potentials (MUAP) [10] over time and space in many muscle fibers [10]. EEG signals are an overall reflection of the electrophysiological activity of the cranial nerve tissues on the surface of the cerebral cortex. Specifically, Local field potentials as electrophysiological signals characterizing brain activity are able to manifest differences in different functionally impaired brains. During Parkinson's disease, the coordination of one's muscles are disturbed. Therefore, studying EMG patterns is an effective tool. EEG signals are an overall reflection of the electrophysiological activity of brain nerve tissue on the surface of the cortex, so analyzing brain structure can help better elucidate the principles of brain waves. This paper will elaborate the relationship between biological signals and PD in detail.

2.1. Local field potential (LFP)

The local field potential represents the sum of the electrical signals of the neurons in the local region of the electrode. When cells are stimulated by substate, the membrane channels partially open, producing weak electrical changes on both sides of the membrane. Thus, the local potential can be either a depolarized potential or a hyperpolar potential. The local potential is formed by different ion flows on different cells, which flow along the concentration difference without energy expenditure. The local field potential has high background noise, low amplitude, which is a very random non-stable signal. The significant reduction in intrastriatal dopamine levels from degenerative death of nigral dopaminergic neurons and the resulting imbalance in neural activity at the basal ganglia are the direct cause of Parkinsonism. A large number of studies show that in the process, the nuclear group at the basal ganglia produces abnormal neural electrical activity, mainly manifested as abnormal oscillation phenomenon [11].

Chen Yue et al. [12] found that changes in different rhythms of the LFP can represent some state of neuronal activity, or be associated with disease, or with brain function. The discovery of LFP biomarkers is most typical in motor disorders. Although the same nucleus as observed in PD, dystonia exhibits different rhythms. Neuronal activity in the sub-halamic nucleus is closely linked to symptoms and their treatment in patients with Parkinson's disease [13].Zhang Kun et al. [14] found neural fluctuations in the subthalamic nucleus of PD with high synchrony and regularity. Excessive synchronization of nerve fluctuations in the frequency band (10~30Hz) of the local field potential in the subthalamic nucleus is closely related to symptoms such as bradykinesia and muscle stiffness. The results of Shenghong He [15] showed that the average sensitivity of autonomous motion detection was 76.8%~88.6%, the number of false positives was 16.0% to 23.1%, and the accuracy of postural tremor was similar. The closed-loop DBS triggered by tremor detection had a suppression rate of 90.5% and the number of false positives was 20.3%.In their previous study, local field potentials (LFPs) recorded from the ventral medium (VIM) thalamus were used to decode autonomous movements and potential tremors, with good offline decoding accuracy. Wang Zongbao [16] investigated the relationship between the local field [17] potential in the subthalamic nucleus in [17] the neural fluctuation components in tremor and resting Parkinson's disease states, and found the harmonic phenomenon of "m tremor frequency" in the local field potential power spectrum of the tremor state in patients (m=1,2,3).The Granger causal analysis shows that the generation of high frequency doubling components is related to the nonlinear coupling between low frequency doubling components. It also confirms that the multiple fluctuating components of tremor-related basal ganglia activity are not independent, and there is a linear and nonlinear interaction between each other, further revealing the complex neural mechanism of tremor occurrence.

2.2. Electromyographic signal

Electromyography (EMG) is the motor unit action potential (MUAP) in muscle fibers. Surface electromyography (sEMG) is a one-dimensional voltage time series signal received by the neuromuscular system, such as surface electrode guidance, amplification, recording and display signal. It is the result of the joint action of superficial muscle electromyography and skin surface nerve stem electrical activity. Electromyography can reflect the activity of nerve and muscle to a certain extent. The sEMG has safe, noninvasive, painless, reliable, objective quantification, and real-time dynamic multi-target evaluation advantages, can make up for the traditional needle pole EMG invasive and not dynamic evaluation in functional activities, for the neuromuscular disease diagnosis, evaluation and treatment plan has important reference value and guiding significance. However, because of the surface electrode, it can only evaluate the superficial muscles, and it is difficult to avoid electrical interference phenomenon, low spatial resolution, cannot accurately distinguish the target muscles and adjacent muscles, so it is difficult to evaluate for the muscles with deep position or small size. SEMG has important practical value in detection of Parkinson's disease.

The advantages and limitations of sEMG evaluation technology is well known, Parkinson's disease resting EMG activity level is significantly higher than the same age, mainly manifested by sEMG signal amplitude [4], muscle burst discharge phenomenon (burst muscle discharges, BMD) increased, and normal active and antagonistic muscle have positive correlation, and Parkinson's disease patients the symptoms of heavier side correlation disappear. The first study of intraoperative surface EMG biomarkers to quantify and predict the efficacy of intraoperative DBS in patients with Parkinson's disease with resting tremor was conducted by Kai-Liang Wang [18].The clinical improvement rate (IR) of the tremor scale was significantly correlated with three significant sEMG biomarkers [18] : peak frequency power (R=0.37, p=0.03), weighted rms (R=0.42, p=0.01), and corrected average amplitude power (R=0.48, p=0.003).These are used to form a Gaussian process regression model with an uninterrupted cross-validating procedure [18].The predicted values of the trained surface EMG prediction model [18] (1000 permutations, p=0.003) correlated well with the true IR of the tremor scale (r=0.47, p=0.0043) [18].Levin et al. [19] found that stiffness is caused by changes in muscle activity and not by muscle structure. Zhang Jie et al. [20] collected 15 patients with PD for EMG tremor analysis, and recorded tremor frequency at resting, fixed posture, 500 g and 100 g 100 g, respectively. It is known that EMG tremor analysis can identify PD by different tremor frequency and muscle contraction patterns. Breit S et al. [21] used a long-term electromyography to track 8 tremor parameters, and using logistic regression, they established a linear formula based on tremor incidence, mean tremor frequency, and phase standard deviation, predicting the correct diagnosis of 93% of patients [21]. The new group of patients received a 100% correct diagnosis in the early stages of the tremor disease model [21]. Long-term EMG records are known to distinguish between Parkinson's disease and idiopathic tremor [21].Ahmed M. Elbeshbeshy et al. [22] studied the time-frequency representation of electromyography (EMG) and compared the performance of pre-trained convolutional neural network models, namely Google lezenet and AlexNet [22], with accuracies of 92.71%, 90.63% and 87.5% [22], separately. Furthermore, data augmentation techniques for the raw EMG [22] signal and its time-frequency [22] representation level help to improve the accuracy of GoogLeNet to 96.88% [22].

2.3. EEG signal

EEG signals are an overall reflection of the electrophysiological activity of brain nerve tissue on the surface of the cortex, so analyzing brain structure can help better elucidate the principles of brain waves. Changes in electrical signals during brain activity the activity data can form an EEG. The EEG reflects the sum of a large amount of neural cell activity. The EEG signals generated by individual neural cells are very weak, so that different amplitudes at different frequencies can be generated in the cerebral cortex. The EEG exam currently plays a crucial role in the clinical diagnosis of neuropsychiatric services. It has been found that Parkinson's diseases related to abnormalities.

The EEG signal features commonly used for Parkinson's detection are mainly frequency features, nonlinear features, etc. Frequency characteristics, Chen Haibo [23] study showed that slow wave activity increased while fast wave activity decreased, especially in patients with PD dementia. It suggests that increased slow wave activity may be an early manifestation of cognitive impairment in PD. It can be considered that qEEG is one of the effective means to assess the cognitive function in PD patients. In terms of the nonlinear characteristics, previous research [4] indicates that EEG signals are complex and nonlinear in nature, and as a result, many linear feature extraction methods fail to accurately characterize these signals. An aggravation of PD is observed when the EEG signal shows complexity. This is due to the presence of a nonlinear component in the EEG signal. Therefore, it should be noted that the use of non-linear drawing techniques will help distinguish between normal and PD EEG signals. The CAD system is an automated detection system for the objective diagnosis of Parkinson's disease using the EEG signal. It is easy to identify the functions of the cortical and sub-cortical portions of the brain [4].The Shu Lih Oh and Yuki Hagiwara [4] studies suggest that computer-aided diagnostic (CAD) systems may help early detect any abnormalities. Because the human brain is a strong nonlinear system, and in the past it used basically linear analysis methods, such as spectrum, no breakthrough has been made in the processing process of brain information and its functional state. Recent developments in nonlinear science provide a powerful tool for studying the human brain. But at present, it mainly uses: correlation dimension and synergy method [24]. Analyzing Parkinson's disease by the complexity measure (Kolmogorov complexity) method has good results and is consistent with the medical statistical view.

Table 1. Comparisons of different physiological signals used in the diagnosis of PD.

Signal	Main characteristics (basic principles applied to Parkinson's detection)	Merits	Demerits
LFP	The low frequency LFP is usually divided into five rhythms: Delta (0 ~ 4 Hz) rhythm, Theta (4 ~ 8 Hz) rhythm, Alpha (8 ~ 12 Hz) rhythms, Beta (12 ~ 24 / 30 Hz)rhythms, Gamma(24/30~40/80Hz)rhythms. Abnormal neural activity in the thalamic nucleus of PD patients is closely related to disease symptoms, in which oversynchronous beta frequency band (12-30 Hz) activity is an important factor leading to slow movement such as symptoms and muscle stiffness.	The modal signal has high amplitude, low randomness, high regularity, and large wavelet packet coefficient.Electrical stimulation inhibition-activity relieves PD symptoms.	The modal signal has high amplitude, low randomness, high regularity, and large wavelet packet coefficient.
EMG	The resting mood level of Parkinson's disease is significantly higher than ordinary people, mainly manifested by surface EMG signal amplitude, increased muscle burst discharge phenomenon (muscle burst, BMD), and positive correlation between normal activity and antagonistic muscles.	Safe, noninvasive, painless, reliable, objective quantified, real-time dynamic multi-target evaluation can compensate for traditional invasive and non-dynamic evaluation.	Due to the presence of surface electrodes, it can only evaluate superficial muscles, it is difficult to avoid electrical interference phenomenon, low spatial resolution, and cannot accurately distinguish between target and adjacent muscles, so it is difficult to evaluate deeper or smaller muscles.
EEG	Main changes of frequency characteristics: normal adult EEG in a quiet, awake, closed eye and relaxed state, the basic rhythm of EEG is 8-13Hz rhythm, wave amplitude of 20-100 V, mainly distributed in the occipital and neck.The frequency of activity is 14-25Hz, and the wave amplitude is 5-20 V, mainly in the frontal and temporal lobes, and some normal people can see a small amount of 4-7Hz waves in the anterior part of the cerebral hemisphere.The frequency below 4Hz is called wave, in the awake normal adult almost no wave, but after falling asleep, and when sleep from shallow to deep wave will gradually increase, if the frequency below 8Hz brain wave is called slow wave.It suggests that the increased slow-wave activity may be an early manifestation of the cognitive impairment occurring in PD patients. Main changes of the nonlinear characteristics: Associated dimension (D2), Point correlation dimension (PD2), The Lyapunov Index (L1), Mogonov wife (K2)	The MEG can record both spontaneous and evoked brain activity.No damage to the human body.The signal is easily available and has a high temporal resolution, no side effect ,the development cycle is short, safe detection process.	Insufficient spatial resolution, the equipment is expensive.

3. Machine learning methods

Machine learning uses data or past experience to optimize the performance standards of computer programs, meaning that computers have the same learning behavior as humans, can gain experience and law, and constantly improve system performance. Machine learning mainly includes Artifificial neural network (ANN), K-nearest neighbor classifier (K-NN), support vector machine (SVM), random forest, deep neural network (DNN), multi-layer perceptron, K-mean clustering, and genetic algorithm. The earliest hierarchical machine learning model is the neural network hierarchical model, and machine learning methods have been successfully applied in the fields [1] of congestive heart failure [1], arrhythmia detection and epilepsy recognition. There are many ways to do deep learning. However, these deep learning model structures, etc., need to be trained on large-scale datasets on the computer. Computer-aided diagnosis cannot only [1] serve as an alternative tool to identify PD, but can also help neurologists confirm their findings [1].To the end, Ankit A. Bhurane and Shivani Dhok [1] use electroencephalography (EEG) signals, a simple and convenient [1] way to identify neural activity in patients with PD. At present, machine learning is still a research hot-spot in various fields, and its applications in biometric medicine, medical diagnosis, and computer vision and so on are constantly expanding. Increasing research on PD detection has applied machine learning methods.

3.1. Traditional machine learning methods

Traditional machine learning methods include logical regression (LR), linear discriminant analysis (LDA), support vector machine (SVM), naive Bayes, decision tree (DT), and k-nearest neighbor (KNN)[20].The part applicable to machine learning here is mainly the part of the classifier. There are three main types of machine learning-based classifiers: decision tree, support vector machines (SVMs), and random forest. Decision trees are the more commonly used classifier in modulation recognition, whose main idea is to perform a hierarchical decomposition of complex problems and progress to the next layer by comparing the threshold values of each layer. Artificial neural network (ANN) is an important tool for classifying various diseases using biological signals / images or possibly any one physical parameter.

The genetic algorithm combined with the random forest classifier performs best, reaching an exact value of 95.58% [26].The ANN using the Levenberg-Marquardt algorithm was found to be the best classifier, with the highest classification accuracy (95.89%) [27].The forest penalized attribute (Forest PA) proved to be a promising PD detector with a small number of decision trees and the highest detection accuracy of 94.12% to 95.00%.Pramanik.M, Pradhan. R, et al. [2] proposed diagnostic method consists of a feature selection and classification process. The accuracy can reach 93.84% reached the lowest number of speech features for Parkinson diagnosis. Support vector machines with recursive feature elimination perform better than other methods. Parkinson's diagnosis had the least number of speech features with an accuracy of 93.84% [28].Du Tingting [24] included 77 PD patients and 37 normal subjects, using the support vector machine (SVM) fitting function (radial basis function) for PD diagnosis, and using the final prediction of the SVM optimal parameters optimized by genetic algorithm (GA).With machine learning based on whole-brain cortical thickness, the diagnostic accuracy is 75%.

3.2. Deep learning method

Deep learning model structure has been proposed, which is a recent development in the field of machine learning [30].Deep learning includes: convolutional neural network (CNN), multi-layer neurons based self-coding neural network including self-coding and sparse coding and deep confidence network (DBN), GAN, RNN and so on. However, these deep learning model structures, etc [31], require the training of large-scale data sets. The core idea of deep learning algorithm is: through hierarchical training and nonlinear transformation of unsupervised data, conduct optimization and iterative calculation, and complete the overall adjustment of the network to reach a steady state. Similar to machine learning methods [32], profound machine learning methods [32] are also divided into supervised and unsupervised learning [32]. The different learning models constructed within the different learning environment are quite different [32]. For example, [32] Convolutional neural networks (CNN) are a profoundly supervised machine learning model, while Deep BelieffNets (DBNs) is an unsupervised machine learning model [32].

According to current models of deep learning networks, there are many types that can be broken down into basic and global models [33], and deterministic model based on network connection model, which can be divided into a neighbouring connection, a transverse layer connection and a circular connection depth model [33].The deep learning network model is the intelligent learning method and cognitive process closest to the human brain, and it is also the theoretical foundation for its practical application [33].Ahmed M. elbeshbeshy et al. [22] used a transfer learning end-to-depth learning system in EMG classification. Due to the introduction of fast and high precision, the demand of the system increases sharply [22] Two types of EMG data can be collected only through the mechanical channel EMG electrode [22], and the classification performance of the system is high [22]. The system can be fine-tuned for other binary classification applications [22]. S. Sivaranjini [34] improved the diagnostic accuracy of PD by using the convolutional neural network structure alexnet [35]. MR images are trained and tested through the transmission learning network to provide accurate detection results for clinical diagnosis. The accuracy of the system is 88.9% [36]. The in-depth learning model can help clinicians not only to diagnose Parkinson's, but also to classify the patient population [36]. Shu Lih Oh [4] proposed an automatic detection system of Parkinson's disease (PD) based on convolutional neural network (CNN) [35]. According to the main feature of Parkinson's disease, the gradual degradation of brain motor function, the study designed a 13 layer CNN architecture to overcome the defects of traditional features [35]. It was found that the accuracy of the model was 88.25%, the sensitivity was 84.71%, and the specificity was 91.77%. Therefore, the classification model can be widely used in clinical diagnosis. Srishti Grover et al. [37] combined the input data set with 16 biomedical speech features [37], and the output variable was motorupdrs score. The drups based scoring system is also found to be a better predictor than the drups based scoring system. By using functional brain images [38] to predict the stage of PD disease in patients, the results show that ISTAT is always better than other feature extraction methods [38]. MLP and RF are the most accurate analytical methods for predicting multivariate set learning model and statistics, respectively [38]. Overall, the depth CNN model with vgg16 weight and architecture formed in advance is better than other methods; it captures key imaging features, effectively distinguishes between normal control group and PM patients, and achieves the highest classification accuracy [38].

4. Discussion

Early detection of Parkinson's disease (PD) is the key to its proper treatment. As the disease spreads in patients, so does the patient's quality of life. This paper details the relationship between biological signals and PD. The proposed computerized machine learning diagnostic system can serve as an adjunct for clinicians to confirm PD findings.

Obtaining the ideal characteristic signal from the information-rich local potential signal is a challenge. Stability, accuracy, degree of quantification, and correlation with patient physiological changes are indicators of the practical value of the characteristic values. During Parkinson's, the coordination of the body's muscles is disturbed. Therefore, studying EMG patterns is an effective tool. Compared with needle electrode electromyography, SEMG has the advantages of non-invasive, non-invasive, and simple measurement operation [8].Under different diseases, or under different symptoms of the same disease, the different rhythms of LFPs in different functional nuclei or brain regions contain a wealth of information [12]. Unearthing the meaning behind this information is of great significance for studying brain function and verifying the mechanism of related diseases. Surface EMG has the advantages of safety, non-invasive, painless, reliable, objective quantification, real-time dynamic multi-target evaluation, etc., which can make up for the invasive and non-dynamic evaluation of traditional acupuncture emulsion, and has important reference value and guiding significance for the diagnosis, evaluation and treatment of neuromuscular diseases. The disadvantage is that due to the presence of surface electrodes, it can only evaluate superficial muscles, it is difficult to avoid electrical interference phenomena, the spatial resolution is low, and it is impossible to accurately distinguish between the target muscle and adjacent muscles, so it is difficult to evaluate the muscles with deeper positions or smaller sizes. The maximum accuracy of using these features of EEG signals to diagnose Parkinson's disease was 99.1% [39]. The method could serve not only as an alternative tool for diagnosing Parkinson's disease, but can also help differentiate other neurological disorders and could help neurologists confirm his findings [1].Moreover, this method can be applied effectively in areas such as computer-assisted congestive heart failure, arrhythmia detection [1], detection of hepatocellular carcinoma, positive volumetric pump estimation [24].

Considering about the machine learning methods that used in the diagnosis of PD, it can be found that the traditional machine learning methods are easier to construct good classifiers, while deep learning methods assume more model parameters, model formation is thus more challenging. the greatest number of model parameters, the greatest amount of data required to participate in the training, and the greatest degree of precision in the early stage diagnosis of Parkinson's disease. The classification model developed through CNN can be used in a large population before clinical [35] use and produce an objective and better patient population classification in the near future [4].Deep learning methods have good results, but low interpretability, and they tend to construct interpretable deep learning models in the future.

5. Conclusion

In conclusion, this research gave a detailed analysis on the physiological signals (including LFP, EMG and EEG) and the machine learning methods (including the traditional machine learning methods and the deep learning methods) that can be used in the diagnosis of Parkinson’s disease. Specifically, the advantages and disadvantages of afore mentioned signals, the issues that should be considered when using machine learning methods in PD detection were analyzed. This research might provide theoretical and practical reference to the accurate diagnosis of PD in the future.

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