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Advances in Clinical Research of Imaging Technology for Parkinson's Disease

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Abstract

Parkinson currently lacks effective indicators for early diagnosis. The cause of the disease is mainly related to the degeneration of dopaminergic neurons in the dense part of the substantia nigra. By studying the changes in the substantia nigra, early Parkinson's patients can be diagnosed by MRI, Ultrasound and Imaging techniques such as positron emission tomography. They have demonstrated the substantia nigra degeneration of Parkinson's patients through many studies. This article reviews the research status of imaging techniques in the diagnosis of Parkinson's disease, and hopes to provide more reliable basis to detect Parkinson's disease.

Keywords

Parkinson's Disease, MRI, Ultrasound, Positron Emission Computed Tomography

1. Introduction

Parkinson's disease (PD), also known as idiopathic Parkinson's disease, is a middle-aged and elderly neurodegenerative disease with an incidence rate second only to Alzheimer's disease [1] [2] [3]. According to epidemiology, the prevalence rate of people over the age of 65 in China is as high as 1.7% [4], and as the population ages, the incidence rate is also increasing year by year [5], which brings serious problems to people's lives. PD is a degenerative disease of the central nervous system. The cause of the disease is still unclear. It is believed that it may be related to genetic inheritance, environment, oxidative stress and other factors [6]. There are no typical early clinical features, and the clinical manifestation is mainly a series of exercises. The neurological symptoms of the extrapyramidal system with non-motor [7], motor symptoms mainly include

resting tremor, bradykinesia, muscle rigidity, etc. The non-motor symptoms mainly include mental disorders, autonomic dysfunction, sensory disorders, sleep disorders, etc. [8]. The quality of life of patients after the disease will be reduced to varying degrees, a variety of complications in the later stage of the disease, severe cases or even disability, poor prognosis [9], which greatly affects the quality of life of patients.

The main cause of motor performance of Parkinson's disease can be attributed to the progressive loss of dopaminergic neurons in the dense substantia nigra innervating the basal ganglia and degenerative death [10]. The pathogenesis is related to many factors, and it is believed that the remaining neurons Acidic inclusion bodies aggregate to form a Lewy body composed of the soluble protein α-synuclein (*α*-syn), whose gene mutations are related to the pathogenesis of hereditary PD [11], neurotrophic factors, neurotransmitters, neuroinflammation, mitochondria Autophagy and other mechanisms can cause progressive degeneration of dopaminergic neurons, leading to the pathogenesis of PD.

Parkinson's disease currently lacks effective biomarkers and treatments for early diagnosis. It is mainly based on empirical diagnosis. There are new revisions to the diagnostic criteria for PD in China and abroad every year. Early diagnosis and early intervention of PD patients are still difficult for PD treatment. Clinically, it is mainly based on clinical manifestations and responses to dopaminergic drugs. Therefore, efforts are still needed to find markers and gold standards for the diagnosis of PD. The damage of dopaminergic neurons in the substantia nigra is considered to be the key to the pathogenesis of PD. Early identification of changes in the substantia nigra may help in the early diagnosis of PD. Imaging is also actively conducting various studies to explore new diagnostic techniques to assist in the diagnosis of PD. The following is a review of the clinical application of imaging technology in PD examination.

2. Magnetic Resonance Imaging

Nuclear magnetic resonance imaging (MRI) is a bio-magnetic spin imaging technology that uses the characteristics of atomic spin motion to generate a signal after an RF pulse excitation in an external magnetic field. It is detected by a detector and input to a computer. After processing, it is converted on the screen image is displayed on the screen [12]. Cheng Qingqing [13] used quantitative magnetic sensitivity imaging (QSM) and R2 imaging to evaluate abnormal iron distribution in specific areas of the brain of PD patients. The study sample included 25 Parkinson's disease patients and 28 healthy volunteers who were age-matched during the same period. The indicators are the magnetic susceptibility and R2 value, namely the susceptibility and R2 value of the dark gray nucleus. The research results show that the sensitivity value of the putamen of Parkinson's disease is significantly increased, while the sensitivity values of the substantia nigra and red nucleus are significantly lower than those of the normal; only an increase in R2 value was observed in the substantia nigra of patients with Parkinson's disease. The results of the study indicate that QSM and R2

mapping can be used to determine the iron level in the human brain. QSM provides a more sensitive method for evaluating abnormal iron distribution in PD patients.

He Wang [14] studied the detection of early PD patients by magnetic resonance diffusion tensor imaging (DTI) imaging. The study sample included 40 early PD patients and 20 healthy volunteers. Through DTI imaging, FA, ADC and MD value were obtained. The results of the study showed that the FA value of the substantia nigra of patients with early PD was significantly reduced. The reason for the analysis may be due to the destruction of neuronal axon integrity and the loss of dopaminergic neurons; ADC and MD values were not significantly different from the Parkinson's patient group. Indicating that ADC and MD values may be less sensitive to the microstructure of brain tissue in patients with early Parkinson's disease. If patients with advanced Parkinson's disease are studied, ADC and MD values may change.

Chen Kunming [15] explored the imaging characteristics of WMH in patients with Parkinson's disease and the relationship between WMH and clinical grading. The study sample included 50 patients with PD. According to the Hoehn & Yahr classification, PD patients were divided into two groups , Mild symptom group (H & Y clinical grade ≤ 2.5 grade) and symptomatic reorganization (H & Y clinical grade ≥ 3 grade) and 45 healthy volunteers of similar age at the same period, the research indicators were T1-weighted and T2-weighted, 28 cases occurred in Parkinson's patients WMH (WMH: T2 weighted high signal, proton weighted, FLAIR sequence high signal, T1 weighted image does not show or slightly lower signal), WMH occurred in 25 cases of healthy people, the difference between the two was not significant, WMH in healthy people and PD patients The average age of positive patients is higher than that of WMH negative patients. Studies have shown that increasing age is a potential risk factor for WMH, and the author also suggests that the most relevant risk factor for WMH is cardiovascular disease.

Guan Xiaojun [16] based on the close relationship between iron deposition in the dorsal and lateral regions of the substantia nigra and the loss of dopaminergic neurons [17], studied the diagnosis of Parkinson's disease by quantitative magnetic sensitivity map (QSM), and believed that PD patients have QSM The substantia nigra "swallow tail sign" disappeared. The study sample included 76 Parkinson's patients and 47 healthy volunteers. The main indicator of the study was T2 * weighted angiography (ESWAN). The QSM map was obtained after ESWAN image processing. The results of the study showed that normal The population's low magnetic susceptibility is manifested as a thin strip or oval low signal, which may be due to the low iron content in the dorsal and lateral regions of the substantia nigra, and the high magnetic susceptibility of patients with Parkinson's disease is manifested by the disappearance of the low signal, that is "The swallowtail sign" disappeared may be due to the obvious iron deposition in the dorsolateral region of the dense substantia nigra. Studies have shown that most patients with Parkinson's disease have the "swallowtail sign" disappear in

the dorsolateral region of the dense nigra.

Li Guo [18] based on MRI-based voxel morphology (VBM-MRI) technology to study the gray matter changes in PD patients, the study sample includes 28 PD patients and 32 healthy volunteers, the research indicators are VBM-MRI images The results of the study showed that compared with the healthy control group, VBM-MRI showed that patients in the PD group had reduced brain gray matter volume in the following brain regions: frontal lobe (bilateral frontal gyrus, left frontal gyrus), bilateral temporal lobe (superior temporal gyrus, mid-temporal gyrus), right cingulate gyrus, right thalamus, bilateral caudate nucleus, and inferior parietal lobules. The PD group had significant reductions in the gray matter volume of the brain in the following brain regions: frontal lobe, temporal lobe, and cingulate gyrus. This indicated that the PD group had more severe frontal, temporal, and cingulate in juries.

3. Ultrasound

Ultrasound research on Parkinson's patients is based on transcranial sonography (TCS) technology. TCS is a convenient, non-invasive, high-availability, and highly repeatable diagnostic method. Many scholars have adopted Cranial measurement of substantia nigra echo for diagnosis, Xu Renfan [19] studied the diagnostic application of TCS in the evaluation of substantia nigra echo area in PD patients. The study sample included 278 PD patients and 300 healthy controls. TCS imaging was used to measure the size of the substantia nigra echo area in PD patients and healthy control groups, and the SN superechoicity was measured (the expansion of the SN echo area is considered to be related to the SN area The increase in iron concentration is related to the increase in SN echo only in approximately 10% of healthy volunteers, so it can be used for early diagnosis of PD patients, SN+), the study results show that the detection rate of SN+ is 90.3% (Reader 1), 89.6% (Reader 2), indicating that SN+ can be used as a stable indicator for PD diagnosis. Studies have shown that the cause of SN+ in PD patients may be increased iron concentration in the tissue, which produces oxidative stress, and SN shows a high echo signal .In healthy individuals, the iron content is low and the echo area of SN is small.

Dong Yanxia [9] studied transcranial color Doppler ultrasound for the determination of substantia nigra echo in PD patients. The study sample was 70 patients with Parkinson's disease, which were divided into group A (course of disease < 5 years), group B (course of disease > 10 years), and during the same period, 30 healthy volunteers were compared. The research index was the mid-brain horizontal cross-section. The area of interest with a diameter of about 0.3 cm was selected to measure the average gray value of the oval substantia nigra area outside the brain. The research results showed that B The gray value of the substantia nigra in the group was significantly larger than that in the group A and the control group. The gray value of the substantia nigra in healthy patients was less than that in patients with Parkinson's disease. Studies have shown

that as the course of Parkinson's disease prolongs, the gray value of the substantia nigra in patients with Parkinson's disease will gradually increase.

Zhang Xunjuan [20] selected 70 Parkinson's patients and 60 healthy subjects in the same period as the study sample. The research index was a mid-brain horizontal cross-section, they selecta circular area of interest with a diameter of about 0.3 - 0.5 cm, and measure the average gray value of the oval substantianigra on the outer side of the brain feet. The results of the study showed that the black matter gray value of Parkinson's patients was significantly higher than that of healthy subjects. The black matter gray value of Parkinson's patients had nothing to do with age and was positively correlated with the course of disease.

4. Positron Emission Computed Tomography

Positron Emission Computed Tomography (PET) is a relatively advanced inspection technology in imaging medicine. It is a kind of functional imaging technology that has developed rapidly in recent years. It can qualitatively and quantitatively reflect the changes of related substances in the body through highly selective and highly specific tracers. The principle is that a substance, generally a substance necessary for the metabolism of biological life, is labeled with short-lived radionuclides (such as Fluorine 18, carbon 11, etc.), introduced into the human body *in vitro*, through the accumulation of the substance in the target organ of the tissue, to reflect the metabolic activities of life, so as to achieve the purpose of diagnosing diseases [21] [22] [23]. Based on ^{18}F-DOPA PET brain imaging to obtain Parkinson's syndrome-related brain metabolism network model, the establishment of automated diagnostic procedures can well diagnose PD at the individual level, providing a powerful tool for early diagnosis and treatment of people at high risk of PD to create favorable conditions for further research on the pathogenesis and treatment mechanisms of neurodegenerative diseases.

The earliest radionuclide used for PET imaging to evaluate the synthesis of dopamine in the substantia nigra cells is 6-18F-fluoro-L-dopa (^{18}F-DOPA), which is often used in the diagnosis of Parkinson's disease. Luo Ganhua [24] studied the diagnosis of Parkinson's disease after improving the effect of ^{18}F-DOPA PET/CT imaging by this Ntacapone drug. The study sample included 44 cases of confirmed PD Patients, of which 24 patients took entacapone before imaging (PDl group), 20 patients did not take entacapone before imaging (PD2 group), and 14 healthy subjects were divided into a control group 1 (6 Subjects took entacapone before imaging) and control 2 groups (8 subjects did not take entacapone before imaging). ^{18}F-DOPA PET/CT imaging was performed. The study results showed that the PD1 group was more clearly developed than the PD2 striatum, and the control group 1 was more clearly developed than the control 2 group, indicating that entacapone can effectively improve the ^{18}F-DOPA uptake; PD patients have different degrees of radioactivity distribution defects on the opposite side of the putamen's putamen, and no radioactivity distribution de-

fects are found in the caudate nucleus. In the control group 1, there is no obvious defect in the radioactivity distribution of the putamen and caudate nucleus. There is damage to the front and back of the bilateral putamen in Parkinson's patients, presumably because the substantia nigra striatum of PD patients has a reduced metabolic level of ^{18}F-DOPA.

Chang Yi [25] studied the value of ^{18}F-DOPA PET imaging in the diagnosis of early Parkinson's disease patients and the evaluation of the severity of Parkinson's disease patients. The study sample was 38 early [Hoehn-Yahr (HY) grade 1 - 2.5] PD patients, and 5 healthy volunteers, studied and analyzed the intake of ^{18}F-DOPA by the striatum and calculated the striatum-occipital lobe intake ratio (SOR). The analysis results show that ^{18}F-DOPA is specifically concentrated in the bilateral basal ganglia of the subjects, but the distribution of scalp is higher in healthy people), PD patients with bilateral putamen ^{18}F-DOPA intake is reduced compared with the control group, the onset of contralateral radioactive intake The reduction was more significant, and the radioactivity in the rear of the putamen was more significant. Although the ^{18}F-DOPA uptake in the bilateral caudate nucleus of the PD group was not significantly reduced, the semi-quantitative analysis results showed that the caudate nucleus SOR was significantly higher than that of the control group. The decrease indicates that there is a decrease in dopamine synthesis capacity in the putamen and caudate nucleus, which further proves that ^{18}F-DOPA imaging can be used as a diagnostic indicator for PD patients.

MRI is clear, and the signal level can be directly compared effectively, and the patient can be evaluated more accurately to understand the patient's disease progression. However, there are more contraindications than ultrasound. For example, patients with claustrophobia are not allowed to enter. Patients with pacemakers are not allowed to enter, etc.

The advantages of ultrasound are the convenience of examination, the low cost of examination, and the ability to check the progress of the disease at any time. It has real-time and dynamic characteristics. However, ultrasound examination is greatly affected by the limitation of the cranial bone, and it is difficult to penetrate the bone. Some other lesions could not be detected.

Positron emission computed tomography (PET) imaging is based on ^{18}F-DOPA. ^{18}F-DOPA is a radioactive marker similar to levodopa, which specifically binds to presynaptic dopamine receptors after entering the brain. ^{18}F-DOPA PET imaging can be used to assess the central dopamine function of presynaptic neurons. The advantage is that the production method of ^{18}F-DOPA is fully automated synthesis, easy to operate, and ^{18}F has a long physical half-life, easy to use, and good F-DOPA imaging effect. However, ^{18}F-DOPA imaging has many influencing factors. Drugs or food may affect the distribution in the brain, so it is necessary to prohibit drugs and fasting before the examination. Moreover, the PET equipment is expensive and the inspection cost is high. The inspection operation is more complicated than MRI and ultrasound inspections.

At present, the diagnosis of PD mainly depends on clinical symptoms and the

responsiveness of dopamine instead of drug therapy to diagnose the disease. The rate of misdiagnosis of PD is relatively high [26], and as long as the disease occurs, the disease will only increase progressively with time. Therefore, early diagnosis and early treatment should be advocated for patients with PD to delay the development of the disease [27]. The pathological manifestations of PD patients are mainly dopaminergic neuron degeneration. MRI, ultrasound, PET and other imaging techniques can be used to observe the difference between the substantia nigra imaging of PD patients and normal people, and conclude that there is damage and degeneration of substantia nigra in PD patients. It is important to be able to detect PD patients early. Although there is a lack of uniformity in the diagnostic criteria, the research on PD is still being explored and progressed. It is believed that with the deeper research, the diagnosis of PD patients will become more and more accurate.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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