Advances in the Use of Positronic Radiomolecular Imaging Agents in the Diagnosis of Parkinson's Disease

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Abstract: The objective of this study was to examine the potential of positron radioactive molecular imaging agents for the diagnosis of Parkinson's disease (PD). With the increasing prevalence of aging and the rising incidence of PD, early diagnosis is of paramount importance to enhance the quality of life of patients. In terms of research methods, this study analyzed the application of positron emission tomography (PET) and computed tomography (CT) technology and its combination with positron radioactive molecular imaging agents in the diagnosis of Parkinson's disease (PD), with particular emphasis on the use of glucose metabolism imaging agents, including 18F-fluoro-2-deoxy-D-glucose (^{18}F-FDG). The findings of the study demonstrate that the integration of PET/CT technology with positron radioactive molecular imaging agents offers a comprehensive approach to the diagnosis of PD. This approach provides valuable functional and metabolic information about the brain of PD patients, and enables the accurate localization of lesions with high specificity and sensitivity, making it a highly effective and well-tolerated diagnostic tool. The utilization of positron radioactive molecular imaging agents in the diagnosis of PD has the potential to significantly enhance the accuracy and efficiency of diagnosis, thereby facilitating early detection and treatment of PD.

Keywords: Computed Tomography; Contrast Agents; Parkinson's Disease; Clinical Diagnosis

1. Introduction

In recent years, China's aging population has become a significant concern, with the incidence of Parkinson's disease in China continuing to rise. Currently, the clinical diagnosis of Parkinson's disease is more prevalent, but due to the patient's In the early stages of the disease, the typical clinical symptoms may not be present. In the clinical diagnosis, clinicians combine their own experience with the patient's clinical manifestations and past history to make a judgment. The diagnostic criteria for Parkinson's disease in the brain histopathology section are not entirely accurate. However, the technical requirements for a pathology biopsy from the doctor are relatively high, which may also cause trauma to the patient's body. The location of the material and the number of requirements is relatively high, which may affect the patient's acceptance. The search for safe, effective, specific, and sensitive diagnostic methods for early diagnosis of Parkinson's disease and early treatment is of great importance [1]. This study focused on the analysis of positron radiomolecular imaging agents in the diagnosis of Parkinson's disease.

2. Parkinson's Disease

Parkinson's disease (PD) is a neurodegenerative disease with a very high incidence. It is also often called tremor paralysis. The disease is mostly found in the middle-aged and elderly groups, especially after the age of 60 years old. The risk of suffering from PD is significantly higher in this age group [2]. The patient's condition is due to pathological changes in the nigrostriatal pathway. The decline in dopamine secretion in

the striatum, the inability to inhibit the function of acetylcholine, and the subsequent breakdown of equilibrium in the patient's neurological function are all consequences of the cholinergic neuron influence on acetylcholine excitability enhancement, resulting in extrapyramidal function hyperactivity [3]. In the case of PD patients, the aforementioned symptoms manifest after the onset of clinical symptoms, which are mainly manifested as a decline in language function, limbs, and part of the body tremor. The incidence rate of PD is very high, and patients experience varying degrees of disability. The condition is characterized by an invisible attack, progressive aggravation, and a lack of effective clinical treatment. The onset of clinical symptoms is primarily manifested as a decline in language function, limb function, and the occurrence of tremors in specific body parts. The incidence rate is exceedingly high, and patients who experience the onset of the disease often exhibit varying degrees of disability. The condition is often described as an "invisible attack" that progresses over time, making it challenging to achieve a favorable prognosis through clinical treatment. Patients with Parkinson's disease (PD) who do not receive timely treatment may experience limited mobility and a decline in quality of life. In the advanced stages of the disease, prolonged bedridden patients are at an increased risk of developing urinary tract infections and pneumonia, which are significant contributors to mortality in PD patients. Statistical data indicates [4] that the number of patients diagnosed with Parkinson's disease (PD) in China has reached 5 million, representing 50% of the global PD patient population. Of this, 3% to 5% are individuals over the age of 70. In the study by Jiang et al.[5] and other research, it has been demonstrated that the onset of Parkinson's disease is closely related to genetic predisposition, age, the environment, and other factors. Following the onset of the disease, patients experience a range of symptoms, including motor, autonomic, cognitive, sleep, and olfactory disturbances. In fact, 24% of patients exhibit these non-motor symptoms at the time of initial consultation. Anecdotally, patients have been found to exhibit autonomic, cognitive, and other non-motor symptoms at the time of their initial consultation. As the disease progresses, the proportion of patients with these symptoms increases. Among patients with the disease, 50% have reached this stage, with 3% to 5% being over 70 years old. As the disease progresses, the condition worsens. It is estimated that 75% of patients will develop Parkinson's disease dementia.

3. PET/CT Diagnostic Technology

In recent years, the continuous development of analytical imaging technology has led to the widespread use of PET/CT diagnostic technology in the diagnosis of a variety of diseases. PET diagnostic technology, which employs molecular imaging equipment, functional imaging, CT structural imaging, and a combination of the two, has not only expanded the scope of medical imaging diagnostic technology beyond pure anatomical and structural changes in imaging diagnosis. Furthermore, PET can be transformed into a functional metabolism. In the diagnosis of diseases, PET can provide doctors with functional, metabolic, and a variety of molecular information. With the help of CT, the anatomical parts of patients can be observed more clearly. Image fusion can accurately locate lesions and characterize them in a single acquisition [6]. In the study by Deng et al.[7], it was demonstrated that PET/CT imaging technology can identify biomarkers associated with the onset and progression of neurological disorders, particularly in the early detection of challenging neurological lesions. This technology offers significant advantages in this area. This diagnostic technology integrates two technologies, PET and CT, with complementary advantages and disadvantages. It not only improves the accuracy of localization but also enhances sensitivity and specificity. Currently, PET/CT has been widely used in the diagnosis of the nervous system, inflammation, tumors, cardiovascular diseases, and other conditions. It can also determine Alzheimer's disease, multiple system atrophy, PD, and other neurological diseases. The rapid development of molecular nuclear medicine has led to the emergence of a variety of new types of positron-emitting radioactive molecular imaging agents, which further enhance the advantages of PET/CT diagnostic

technology in the early diagnosis of PD disease. In the diagnosis of PD disease, positron-emitting radioactive molecular imaging agents should be combined with receptors, neurotransmitters, and transport proteins in the brain. The anatomical structure of the patient can be accurately observed to determine whether there is any change with the help of PET/CT visualization. The use of PET/CT imaging allows for the accurate observation of anatomical structure, the determination of abnormal changes in function and metabolism, and the timely assessment of patient condition. This diagnostic method is convenient and simple to operate, with a high degree of specificity and sensitivity.

4. Positron Radiomolecular Imaging Agents

4.1 Glucose Metabolizing Agents

^{18}F-Fluoro-2-Deoxy-D-Glucose (^{18}F-FDG), a deoxyglucose analog, is a widely utilized radiopharmaceutical in positron emission tomography (PET) and computed tomography (CT) imaging. Glucose is an essential energy substrate for the body, and by observing glucose metabolism in the body, it is possible to determine whether there is This indicates an abnormal change in the patient's function. In patients with Parkinson's disease (PD), the metabolism of ^{18}F-FDG has decreased due to the disease, and the metabolism of the striatum is asymmetrical on both sides. In contrast, the metabolic level of the thalamus, nucleus pulposus, and brainstem of patients has increased significantly. The metabolic processes of PD patients exhibit asymmetry, with elevated metabolic levels observed in the thalamus, nucleus accumbens, and brainstem. Abnormal metabolism of the nucleus accumbens is associated with motor retardation, and as the metabolic level of the patient increases, the motor retardation becomes more pronounced. As the condition of PD patients gradually worsens, the metabolic level of the caudate nucleus decreases to a more serious degree, with widespread hypometabolism in the cortical areas. Additionally, the metabolism of the dorsolateral prefrontal cortex and posterior cortex also decreases significantly.It was demonstrated [8] that patients with Parkinson's disease (PD) exhibit severe ^{18}F-FDG metabolic deficits in the posterior hemisphere, parietal lobe, and occipital lobe. These deficits result in cognitive impairments in the patients. Furthermore, low metabolic levels are more pronounced in the posterior parietal lobe and the occipital lobe, particularly in the right angular gyrus, cuneate lobe, and left precuneate lobe. In the case of Na and Mutalbekd emonstrated that the maximum standardized uptake values of the shell nuclei[9], caudate nucleus, thalamus, and the lobes of the brain on both sides of the patient could be observed by ^{18}F-FDG PET/CT images to determine the alteration of the patient's cerebral metabolism. In this study, 107 patients with a preliminary diagnosis of PD and 43 patients with a health checkup were selected. The diagnosis was found to be similar to that of the patients with regard to the severity of the disease and the severity of the ^{18}F-FDG and 11C-CFPET images. The severity of the patients' disease and the decrease in ^{18}F-FDG metabolism exhibited a positive correlation. The patients exhibited high metabolic levels in the thalamus, chiasmatic nucleus, and caudate nucleus, while exhibiting low metabolic levels in the frontoparietal-temporal-occipital lobe. The combination of 11C-CFT PET with ^{18}F-FDG allows for the observation of dopamine distribution and glucose metabolism in brain cells, which is of significant value in the diagnosis of Parkinson's disease. It provides more accurate and objective reference data for the diagnosis of the disease.

4.2 Dopamine Metabolizing Agents

As an analog of the dopamine precursor L-dopa, the injection of ^{18}F-6-fluoro-L-dopa (^{18}F-6-L-FDOPA) into the patient's body allows for the participation of this imaging agent in the dopamine metabolism process of the body. This enables the observation of any abnormal changes in the function of the presynaptic dopaminergic system of the brain of the patient. Studies have demonstrated that patients with Parkinson's disease (PD) often do not exhibit overt striatal changes in the early stages of the disease. However, with the progression of

the patient's condition, the striatum gradually appears to be reduced in radioactivity or even defective. In Yi et al.[10], it was demonstrated that PD belongs to the nigrostriatal-striatal dopaminergic neural pathway degenerative diseases. Once suffering from PD, 50% to 80% of patients exhibited nigrostriatal dopaminergic neuron deletion. However, patients in the early stage of the disease exhibited no obvious change in the striatum. With the aggravation of the disease, the striatum only appeared to have defects and decreased radioactivity.Rather, ^{18}F-6-L-FDOPA can observe the presynaptic dopa desorption enzyme activity in the substantia nigra striata of the patients. Depending on the clinical manifestations of the patients and the number of dopaminergic neurons, the ^{18}F-6-L-FDOPA will show different changes in the PET-CT imaging. At the early stage of the patient's disease, compensatory elevation of dopamine neurons, dopa desorption enzyme activity, and dopamine synthesis occur, accompanied by a decrease in L-dopa metabolism. Consequently, ^{18}F-6-L-FDOPA is not observed in PET-CT imaging at this stage, and the patient's dopamine loss is not evident.

4.2.1 Receptor-based imaging agents

The D_1 and D_2 receptors belong to the dopamine receptor family. The D_1 receptor includes the D_1 and $D_5$2 subtypes, while the D_2 receptor includes the D_2~$D_4$3 subtypes. By modifying the structure of dopamine receptor antagonists and agonists, it is possible to observe the specific location and number of receptors using radiolabeled compounds, which can then be combined with the specificity of dopamine receptors. Currently, dopamine receptor visualizers are better developed in molecular nuclear medicine, with D_2 receptor visualizers playing an important role in the diagnosis of PD. Among them, 11C-Reclopride belongs to the central dopamine D_2 receptor-specific antagonists with very good selectivity and possesses a relatively high affinity in the receptor. Furthermore, ^{18}F-Fallypride is a radiotracer with high affinity and better lipophilicity, which can be quantitatively evaluated for dopamine D_2 receptor alteration in PET-CT visualization. This technique not only analyzes the pathogenesis of Parkinson's disease but also evaluates the effect of patients' medication [11].

4.2.2 Dopamine transporter protein visualizer

The dopamine transporter protein is primarily located in the presynaptic membrane of central dopaminergic neurons. ^{18}F and ^{11}C-labeled cocaine derivatives are imaging agents for the dopamine transporter protein. These agents have a high affinity for the protein and a relatively high specific uptake. However, due to the slower brain clearance rate, they are not ideal for use in humans. Following intravenous injection, the dopamine transporter protein produces a specific binding in the synaptic pre-synaptic dopaminergic neuronal system. This is more intuitive and more sensitive than postsynaptic receptor imaging performance, which was previously the standard. The information obtained from this process can be used to determine the severity of the disease in patients with PD. Currently, dopamine transporter protein imaging agents are not only extensively utilized in the diagnosis of Parkinson's disease (PD), but also exhibit the most optimal diagnostic efficacy.^{11}C-β-CIT has a very high affinity for dopamine transporter proteins, and shows very high affinity for noradrenoceptors and 5-hydroxytryptamine receptors, and does not show high uptake ratios with striatum and peripheral tissues for a short period of time.^{11}C-β-CFT has a lower affinity for dopamine transporter proteins than ^{11}C-β-CIT, but because of the lower affinity for noradrenoceptors and 5-hydroxytryptamine receptors, the uptake ratio of ^{11}C-β-CFT in striatum was not as high as that for dopamine transporter proteins within 20 In striatal uptake, ^{11}C-β-CFT showed a rising trend in 20 min, and the disease was slowly prolonged with time, while in ^{11}C-β-CFT cerebellar uptake, the peak could be reached in 15 min, and showed a decreasing trend after the peak, and the difference in uptake between striatum and cerebellum was relatively high, and very clear images could be obtained after PET- CT scanning, because striatum and cerebellum showed an elevated trend in ^{11}C-β-CIT community, but the amount of uptake was really not high. However, there

is no significant difference in uptake, and ^{11}C-β-CFT is more advantageous than ^{11}C-β-CIT in the early diagnosis of PD. In a study by Xu et al.[12], ^{11}C-β-CFT PET/CT was performed on 91 cases of PD, APS, and 11 healthy individuals. The results indicated that the degree of dysfunction of the striatal dopaminergic nervous system could be observed using this method. The ^{11}C-β-CFT PET/CT procedure allows for the observation of the degree of nigral damage in patients, and has been demonstrated to be highly efficacious in the diagnosis of neurodegenerative diseases, as well as in the assessment of posterior cistern nucleus uptake values, particularly in the diagnosis of PD.

5. Conclusion

A positron emission molecular imaging agent with molecular biology technology and nuclide labeling technology is a valuable diagnostic tool for Parkinson's disease. It is used in conjunction with PET/CT technology to diagnose patients with the disease. This technology offers high specificity and does not cause trauma to the patient's body. It is particularly advantageous for studying the molecular level of living cells. In the future, nuclear medicine molecular functional imaging research may focus on positron emission molecular imaging research.

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