

Mechanisms and Treatment Strategies of Motor Complications in Parkinson's Disease Patients

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Keywords: Parkinson's Disease; Sports Complications; Treatment Strategy; Drug Therapy; Surgical Treatment

Abstract: The sports complications of Parkinson's disease (PD) seriously affect the quality of life of patients. This article discusses its related contents in depth. This article expounds the pathogenesis of sports complications in neurotransmitter imbalance, neuroplasticity changes, genes and genetic factors and other related factors (age, course of disease, severity of disease, brain inflammation, oxidative stress, etc.). In terms of treatment strategy, drug therapy includes adjusting the dosage, dosage form and frequency of administration of existing drugs such as levodopa, combined application of dopamine receptor agonists, monoamine oxidase -B inhibitors, and auxiliary drugs such as COMT inhibitors, while paying attention to the research and development progress of new drugs. Surgical treatment includes deep brain stimulation (DBS) and other operations such as nucleus destruction, emerging stem cell transplantation and gene therapy. Rehabilitation treatment covers physics, homework, speech therapy and so on. Various treatment strategies have their own characteristics and limitations, and multi-pronged approach is expected to improve the status of patients with PD motor complications.

1. Introduction

As a common neurodegenerative disease, the incidence of PD has gradually increased with the acceleration of the global population aging process [1]. According to epidemiological investigation, the prevalence rate of PD is about 1%-2% among people over 65 years old, and the prevalence rate doubles every 10 years old [2]. The main clinical manifestations of PD are motor symptoms such as static tremor, bradykinesia, myotonia and postural balance disorder, and non-motor symptoms such as hypoesthesia, constipation, sleep disorder and depression [3-4]. Although drugs such as levodopa have a significant effect on improving the motor symptoms of PD patients, with the progress of the disease course and the long-term use of drugs, most patients will inevitably have motor complications, which will seriously affect their quality of life [5].

As a difficult problem in the treatment of PD, sports complications mainly include peak shift, bipolar shift, dystonia and switching phenomenon [6]. These complications not only increase the physical pain of patients, but also increase the burden of caregivers and social medical costs. It is of great significance to explore the pathogenesis of sports complications in PD patients for developing more effective treatment strategies and improving the prognosis of patients.

At present, some progress has been made in the research on the mechanism of PD sports

complications, involving neurotransmitter imbalance, neuroplasticity changes, genes and genetic factors [7]. In the treatment strategy, drug therapy is still the main means, but the development and application of new drugs still face many challenges; Although surgical treatment such as DBS shows certain advantages, it also has limitations; As an auxiliary means, the importance of rehabilitation therapy is gradually recognized [8]. The purpose of this study is to systematically sort out the mechanism of sports complications of PD, and comprehensively analyze and discuss the existing treatment strategies in order to provide more scientific and effective theoretical guidance for clinical practice.

2. Overview of PD and sports complications

PD is a common neurodegenerative disease, which mostly occurs in middle-aged and elderly people. Its main pathological feature is the degeneration and death of dopaminergic neurons in substantia nigra, which leads to a significant decrease in dopamine content in striatum, and then leads to a series of motor symptoms, such as resting tremor, bradykinesia, myotonia and postural balance disorder [9]. With the progress of the disease and long-term drug treatment, patients often have sports complications, which seriously affect their quality of life. Sports complications mainly include symptom fluctuation and dyskinesia. Symptoms fluctuate as "on-off" phenomenon, end-of-drug phenomenon, etc. The "on-off" phenomenon refers to the rapid transition of patients' symptoms between sudden remission (initial period) and aggravation (off period); The phenomenon of drug end is that the effective action time of each drug is gradually shortened. Dyskinesia is characterized by involuntary movements like dancing, hand and foot creep or dystonia, which is common in peak dyskinesia and bipolar dyskinesia.

3. Mechanism of sports complications of PD

(1) Imbalance of neurotransmitters

Table 1 Major Neurotransmitter Imbalances in PD and Their Impact on Motor Function

Neurotransmitter	Imbalance State	Impact on Motor Function
Dopamine	Decreased (in PD itself); Altered receptor function after medication	Symptoms like bradykinesia and tremor; Long-term medication may induce motor complications
Acetylcholine	Relatively increased	Worsens symptoms such as tremor and muscle rigidity
Glutamate	Possible excessive release	Contributes to motor complications like dyskinesia
GABA	Dysfunction	Disrupts motor regulation and participates in the progression of motor complications

The occurrence of PD motor complications is closely related to the imbalance of neurotransmitters. The change of dopaminergic system is the key factor [10]. In the process of PD, dopaminergic neurons in substantia nigra-striatum pathway gradually degenerate and die, resulting in a significant decrease in dopamine release. When levodopa and other drugs are used to supplement dopamine, although it can improve motor symptoms, long-term use will change the function of dopamine receptor. At the same time, the balance between other neurotransmitters and dopamine is also crucial. Taking acetylcholine (ACh) as an example, under normal circumstances, ACh and dopamine antagonize each other to maintain exercise balance. In PD, dopamine decreases, and ACh is relatively dominant, which breaks the balance and causes symptoms such as tremor and myotonia. Table 1 shows the unbalanced state of several important neurotransmitters and their corresponding motor performances. It can be seen from the table that glutamate, as an excitatory neurotransmitter, will overactivate neurons, and the overactivity of glutamate energy system may play a driving role in sports complications, especially when dyskinesia occurs. However, γ

-aminobutyric acid (GABA) is an inhibitory neurotransmitter, and its abnormal function will also interfere with exercise regulation.

(2) Changes of neuroplasticity

There are neuroplasticity changes in the brain of PD patients, which play an important role in the development of sports complications. The synaptic structure and function of neurons change, and the density of dendritic spines changes, which affects the signal transmission between neurons. Long-term use of drugs such as levodopa will interfere with this neuroplasticity. Drug-induced neuroplasticity changes may change the response mode of neurons to drugs, and they can no longer accurately regulate movement, thus promoting motor complications.

(3) Genes and genetic factors

Genes and genetic factors also play an important role in sports complications of PD. Studies have found that some gene polymorphisms are related to sports complications. For example, specific gene mutation may affect the activity of drug metabolic enzymes, change the metabolic process of drugs such as levodopa, lead to abnormal drug concentration fluctuation in the body, and increase the risk of sports complications. There are also some gene variations that may affect the process of neurotransmitter synthesis and transport, making neurotransmitter imbalance more likely to occur, and then causing sports complications.

(4) Other relevant factors

Age, course of disease and severity of disease are closely related to sports complications. Generally, the older, the longer the course of disease and the more serious the disease, the higher the incidence of sports complications. Pathological processes such as brain inflammation and oxidative stress are also related to sports complications. Inflammation may lead to neuron injury and neurotransmitter metabolism disorder, while oxidative stress will damage intracellular biomacromolecules, affect the normal function of neurons and jointly promote the occurrence and development of sports complications.

4. Treatment strategy of PD motor complications

(1) Drug therapy

Reasonable adjustment of existing drugs is a common means for PD exercise complications. Levodopa is the "gold standard" drug for treating PD. Adjusting its dosage, dosage form and frequency of administration can improve sports complications. At the same time, dopamine receptor agonists, such as pramipexole and ropinirole, can be used in combination, which can directly stimulate dopamine receptors, reduce the dosage and fluctuation of levodopa and reduce the risk of dyskinesia. Monoamine oxidase -B inhibitors (such as selegiline and rasagiline) can inhibit the degradation of dopamine and prolong its action time.

Table 2 Effects of Common PD Medications on Motor Complications

Drug Class	Examples	Peak-Dose Dyskinesia	Biphasic Dyskinesia	Dystonia	On-Off Fluctuations
Levodopa	Levodopa & CR	May improve, but long-term use can trigger	Some relief	May worsen	Adjusting formulation/dose helps
Dopamine Agonists	Pramipexole, Ropinirole	Reduces levodopa dose, lowers risk	Beneficial	May provide some relief	Improves
MAO-B Inhibitors	Selegiline, Rasagiline	Helps reduce fluctuations, mild improvement	Some benefit	Unclear effect	Some improvement
Amantadine	Amantadine	Some efficacy	Limited effect	Limited effect	Limited effect

Table 2 shows the effects of several common drugs on different sports complications in detail.

As can be seen from the table, different drugs have their own advantages and limitations for different sports complications.

Auxiliary drugs such as B inhibitor and catechol-O-methyltransferase (COMT) inhibitor also play an important role in the treatment of sports complications. COMT inhibitors (such as entacapone) can inhibit COMT enzyme, reduce the metabolism of levodopa in the periphery, increase the amount of levodopa entering the brain, stabilize the blood drug concentration, and thus improve sports complications. Table 3 further expounds the action mechanism and application characteristics of this kind of auxiliary drugs.

Table 3 Mechanisms and Applications of Adjunctive Drugs in Managing Motor Complications

Drug Class	Examples	Mechanism of Action	Application in Motor Complications	Notes
COMT Inhibitors	Entacapone	Blocks COMT enzyme, increases levodopa bioavailability	Improves wearing-off, reduces on-off fluctuations	May discolor urine; monitor
MAO-B Inhibitors	Selegiline, Rasagiline	Modulates neurotransmitter signaling	Effective for specific motor complications	Consider indications and side effects

At present, the research and development of new drugs for PD sports complications has been continuously promoted. Adenosine A2A receptor antagonist can regulate adenosine A2A receptor, affect neurotransmitter release and neuron activity, and is expected to improve sports complications. Glutamate receptor modulator can correct the imbalance of excitatory neurotransmitters by regulating glutamate energy system, showing potential curative effect. Although these new drugs are in the research and development stage, they bring new hope for the treatment of PD sports complications.

(2) Surgical treatment

DBS is an important surgical method to treat sports complications of PD. Its principle is to stimulate specific nerve nuclei and regulate nerve signal transmission through electrodes implanted in the brain. Surgical targets often choose the medial part of globus pallidus and subthalamic nucleus. Taking subthalamic nucleus as an example, stimulating this part can effectively improve the symptoms of bradykinesia, tremor and myotonia, and also has a significant effect on motor complications. DBS therapy has many advantages, such as reversibility and adjustability, and can adjust stimulation parameters according to patients' symptoms. However, it also has limitations, and the operation has certain risks, such as infection and bleeding. Postoperative program control is also complicated, which requires professional doctors to make multiple adjustments according to the patient's situation. Nucleus destruction has also been used to treat PD motor complications. It can improve symptoms by destroying specific nerve nuclei, but compared with DBS, nerve nucleus destruction is irreversible and may cause more complications.

(3) Rehabilitation treatment

Rehabilitation treatment is very important for patients with PD motor complications. Physical therapy can improve the motor function and balance ability of patients and reduce the risk of falling through exercise training, such as balance training and gait training. Occupational therapy focuses on helping patients recover their activities of daily living, such as dressing and eating. Speech therapy can improve patients' speech and swallowing function, and alleviate problems such as slurred speech and dysphagia caused by exercise complications. Rehabilitation treatment should be based on the individual situation of patients to develop personalized programs, and long-term adherence to achieve the best results.

(4) Integrated management and multidisciplinary cooperation

The treatment of PD sports complications needs comprehensive management and

multidisciplinary cooperation. Doctors, rehabilitation therapists, nurses, nutritionists and other multidisciplinary teams participate together to formulate a comprehensive treatment plan for patients. Doctors are responsible for drug adjustment and surgical evaluation; Rehabilitation therapists provide rehabilitation training guidance; Nurses assist patients and their families in daily care; Nutritionists provide patients with reasonable dietary advice, ensure balanced nutrition and maintain patients' physical function. Health education for patients and their families is also indispensable, so that they can understand disease knowledge, treatment methods and self-management points, and improve patients' treatment compliance and quality of life. Through comprehensive management and multidisciplinary cooperation, it is expected to provide more effective treatment and care for patients with PD sports complications.

5. Conclusions

The research and treatment of sports complications of PD is a complex and sustainable field. From the pathogenesis, many factors are intertwined and jointly promote the occurrence and development of sports complications. Neurotransmitter imbalance, neuroplasticity changes, genes and genetic factors, age, course of disease and other related factors all play an important role, which provides a multi-dimensional perspective for understanding the disease process.

In the treatment strategy, drug therapy is the basic means, and the optimization and adjustment of existing drugs, the rational application of auxiliary drugs and the research and development of new drugs constantly enrich the treatment options, but the adverse reactions and long-term curative effects of drugs still need attention. In surgical treatment, DBS has become an important treatment method because of its unique advantages, but the risk of operation and the complexity of postoperative program control can not be ignored. Although other surgical methods have their own characteristics, they also face many challenges. Rehabilitation treatment has a significant effect on improving patients' motor function and daily living ability, while comprehensive management and multidisciplinary cooperation provide comprehensive support for patients as a whole. In the future, the treatment of PD sports complications needs to further integrate various treatment methods to form a more perfect comprehensive treatment system.

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