# Assessment of Neuropathological Findings and Medical Treatment of Parkinson Disease: A Review of Literature

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## ABSTRACT

***Background***: Parkinson disease is a long-lasting and progressive motor disorder which is identified by three critical motor symptoms which are bradykinesia, rigidity and tremor.

***Aim of the study:*** To assess the histopathological changes in the brain of Parkinson disease's patients and the regimes used for treatment.

***Conclusion:*** Several histopathological changes in the neurons in brain of patients with Parkinson disease are α-synucleinopathies, lewy bodies, damage of synaptic neurons, and hyperactivation of microglial cell. Many regimes were used in the treatment of Parkinson disease particularly to alleviate motor symptoms. The golden goal is they should focus on preserving the synaptic neurons before they get damaged.

***Keywords:*** neuropathology, treatment, Parkinson disease.

# تقييم النتائج المرضية العصبية والعلاج الطبي لمرض باركنسون: مقال مراجعة

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## الخلاصة

**الخلفية :** مرض باركنسون هو اضطراب حركي طويل الأمد ومتقدم يتم تحديده من خلال ثلاثة أعراض حركية خطيرة وهي بطء الحركة والصلابة والرعشة.

**هدف الدراسة :** تقييم التغيرات النسيجية المرضية في دماغ مرضى باركنسون والطرق المستخدمة في العلاج.

**الاستنتاج :** العديد من التغيرات النسيجية المرضية في الخلايا العصبية لمرض باركنسون هي اعتلالات ألفا سينوكلينوبا ، وأجسام ليوية ، وتلف الخلايا العصبية المشبكية ، وفرط نشاط الخلايا الدبقية الصغيرة. تم استخدام العديد من الأنظمة في علاج مرض باركنسون خاصة للتخفيف من الأعراض الحركية. الهدف الذهبي هو أن يتم التركيز على الحفاظ على الخلايا العصبية المشبكية قبل أن تتضرر.

**الكلمات المفتاحية :** أمراض الأعصاب ،العلاج ، مرض باركنسون

## INTRODUCTION

Parkinson disease is an important progressive neurodegenerative disorder that patients may suffer from this illness for the rest of their lives [1]. More than ten million individuals all over the world complaint of this disease which is identified by three critical motor symptoms including bradykinesia, rigidity and tremor [2] but the final diagnosis should be established by histopathological examination and characterization of Lewy bodies formation [3]. The etiology of the disease is idiopathic and it is suggested that genetic mutations in both dominant or recessive inherited genes can play important role in the occurrence of the disease (less than 10%) specifically glucocerebrosidase genes mutations [4]. The environment also has a significant role like aging process as the incidence of the disease is less than 1% in patients aged 66 to70 years and increase up to less than 4% among those above 80 years of age [5].

## Histopathological Assessment

The impact of the disease is on the structure of dopaminergic neurons in the pars compacta of substantia nigra of the basal ganglia which is situated on the dorsal part of the cerebral peduncle in the midbrain with presence of Lewy bodies [6]. In fact, Goldman et al. [7] found that these especial eosinophilic bodies accumulated within the cytoplasm of affected neurons containing especial kinds of proteins and neurofilaments antigens. Kruger et al. [8] found that α-synuclein forming one of the important components of Lewy bodies. Authors reported that α-synuclein is a special type of protein that is normally concentrated in the presynaptic sites [9].

Spillantini et al. [10] reported 6 confirmed cases of idiopathic Parkinson disease and found that α-synuclein antigen is embedded within the structure of Lewy bodies and causes degeneration of neurons.

On the other hand, Hijaz et al. [11] stated that two characteristic features should be found on diagnosis of Parkinson disease, first is the damage of dopaminergic neurons in substantia nigra and second is the deposition of amyloid fibrils proteins that form the α-synuclein and Lewy bodies.

Many experimental studies support the fact that there is an auto propagation process of α-synuclein seeds and any exogenous implementation of synthesized α-synuclein seeds can initiate progressive neurodegenerative illnesses in treated animals [12]. There will be misfolding and auto-accumulation of α-synuclein forming distinctive inclusion bodies named as Lewy bodies [13].

Other experimental studies showed that the neurons that already have α-synuclein when implemented with fibrils this will induce the accumulation of pathogenic α-synuclein aggregations looks like Lewy bodies [14]. In addition to accumulation of this protein in the substantia nigra pars compacta it can be seen also in other sites like brain cortical region and amygdaloid nucleus and hippocampus [15].

Froula et al. [16] conducted their experimental study on mice, they found that accumulation of α-synuclein inclusions within the cytoplasmic neurons will lead to histological and biochemical changes (induction of action on the presynaptic sites, lack of constant dendrites, decrease the calcium transition) in these neurons even before the neurodegenerative process has been started, so researchers now tried to safe these neurons before the degenerative process started.

Kouli et al. [17] studied the postmortem brain tissue of twenty-eight Parkinson disease cases and they found that there is an increase in the number of highly active microglial cell especially in the hippocampus, cingulate and temporal gyri with heavy infiltration with T-lymphocytes inflammatory cell.

The Braak staging suggests that Parkinson disease pathology developes in a stereotypic way in neuroanatomically related sites in the brain [18]. External factors, like pollutants, germs, or inflammatory agents, can enhances lewy bodies pathology in the gastrointestinal nerve cells, or in the neurons of the olfactory bulb. All these might form initial spots for accumulation of α-synuclein inclusions [19].

## Treatment of Parkinson Disease

The treatment depends on the symptoms which are both motor symptoms like tremor, slowness, and rigidity and non-motor symptoms like cognition, sleep disturbances, and gastrointestinal symptoms like constipation, dizziness [20].

Levodopa is the precursor of dopamine and it was first used in seventies of last century and it stills the drug of choice in treatment of Parkinson disease [21]. Later on, other medicines were used like benserazide and carbidopa to decrease the peripheral adverse reactions like nausea, vomiting, and postural hypotension [22]. In the last few years researchers tried to avoid levodopa as first line drug as it has many complications including cognitive disturbances, motor fluctuations, dyskinesia, and dystonia which can be hardly managed [23]. These symptoms can be reduced through intermittent activation of postsynaptic neurons by shortly active form levodopa [24].

Levodopa is actively crosses the blood brain barrier. It should always be given in combination with peripheral Dopa- decarboxylase inhibitors (like carbidopa, benserazide) which do not pass through the blood brain barrier and it is used to decrease its alteration to dopamine at the peripheral sites and it also reduces the peripheral action of L-amino acid decarboxylase, and this may help to reduce the gastrointestinal symptoms [25].

The first dose of levodopa is given in a dose of 300mg/day together with carbidopa in a dose of 75mg/day both are given three times a day but, as the disease progresses the patients need to increase the initial dose to get the same result [26].

When the patient missed the daily dose, no worsening of symptoms can be detected. This is because levodopa is still available in the presynaptic sites but, as the disease progress, the symptoms getting worse due to extensive destruction of the neurons and the patient will suffer from symptoms longer time before the next dose comes [27].

Dopamine agonists are also advised to be given to Parkinson disease. As they stimulate the dopamine action in the brain. They are administered either alone as monotherapy especially in the first stage of the disease or in combination with levodopa, as it may decrease the motor symptoms, fluctuations, and even dyskinesia that is associated with levodopa alone [28] . The most frequently used dopamine agonists which are believed to postponed the necessity to use levodopa are pramipexole, ropinirole [29] .

Furthermore, Anticholinergics were used in treatment of Parkinson disease either alone or in combination with other medicine to reduce the motor symptoms especially the tremor [30] . They can be used in the early stage when the disease is mild and they are beneficial especially for young patients as anticholinergics are associated with many side effects like glaucoma, urine retention, dry mouth, constipation which can be tolerated by young patients. In an elderly patients additional side effects were detected like confusion, hallucination, mood and cognition disturbances [31] . It has been reported that Parkinson disease patients who are chronic users of anticholinergics are more susceptible of developing dementia [32] .

In the last decade, there has been a great interest to include exercise in the rehabilitative program of patients. exercise therapies have been found to have neuroprotective effects and it can inhibit or slowing down the progression of the disease [33,34] .

## CONCLUSION

The most important neuropathological changes in the brain of Parkinson disease are α-synucleinopathies, lewy bodies, damage of synaptic neurons, and hyperactivation of microglial cell.

Many regimes were used in the management of the disease particularly to alleviate the symptoms of muscular disturbances but, the golden goal is to focus on preserving the synaptic neurons before they get damaged.

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