

## Parkinson Disease: review

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### ABSTRACT:

Parkinson's sickness (PD) is a neurodegenerative ailment precipitated by the death of a kind of neuron that plays an integral function in the production of dopamine in the brain. The pathophysiology of this sickness is based totally on the formation of alpha syncline folds that generate Lewy bodies, which are cytotoxic and minimize dopamine levels. Most pharmacological redress for PD goal alphasynuclein to limit the symptoms. However, the therapeutic method to this pathology includes combination of pharmacological and non-pharmacological strategies to maximize results and improve symptomatological manipulate in these patients. It is therefore essential to delve deeper into the pathophysiology of the ailment in order to enhance these remedies and consequently the exceptional of life of the patients. Therefore, we urgently want to analyze every cutting-edge clinical trial's status and therapeutic approach to find out new therapeutic tactics for PD treatment. We hope this evaluate can supply new ideas and insights for PD remedy development.

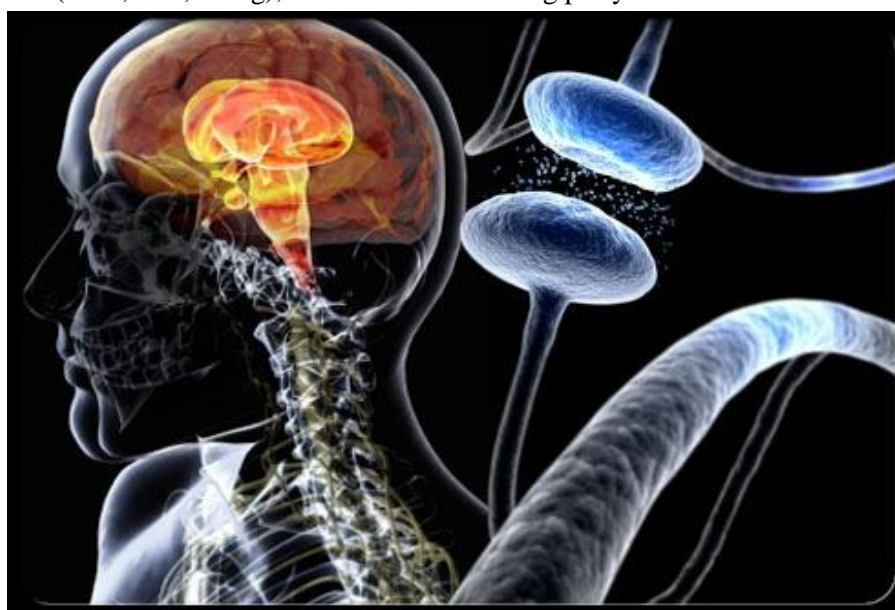
**KEYWORDS:** Parkinson's disease, pathophysiology, therapeutic, remedies, treatment.

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## 1. INTRODUCTION

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Parkinson's disease is a fairly common age-related and progressive disease of brain cells (brain disorder) ( **Figure.1.**) that affect movement, loss of muscle control, and balance. Usually, the first symptoms include a tremor (hand, foot, or leg), also termed a "shaking palsy."



(Figure.1.)

The progression of Parkinson's disease and the degree of impairment vary from individual to individual. Many people with Parkinson's disease live long productive lives, whereas others become disabled much more quickly. Premature death is usually due to complications such as falling-related injuries or pneumonia [1].

Parkinson's disease was named after the British doctor James Parkinson, who in 1817 first described the disorder in great detail as "shaking palsy."

From this time scientists have pursued the causes and treatment of the disease. In the early 1960s, scientists identified the primary problem underlying the disease: the loss of brain cells that produce a chemical called dopamine, which helps to coordinate and control muscle activity. dopamine acts as a messenger between two brain areas and the corpus striatum - to produce smooth, controlled movements [2].

In the United States, about 1 million people are affected by Parkinson's disease and worldwide about 5 million. Most individuals who develop Parkinson's disease are 60 years of age or older. Parkinson's disease occurs in approximately 1% of individuals aged 60 years and in about 4% of those aged 80 years. Since overall life expectancy is rising, the number of individuals with Parkinson's disease will increase in the future. Adult-onset Parkinson's disease is most common, but early-onset Parkinson's disease (onset between 21-40 years), and juvenile-onset Parkinson's disease (onset before age 21) also exist [3].

Parkinson's disease (PD) is a common neurodegenerative disorder with a cumulative effect on patients, their families and the healthcare and social care systems.

In Scotland, there are between 120 and 230 patients with PD per 100,000 people.<sup>1-3</sup> While the population of Scotland remains stable, the age related incidence of PD means that the number of cases will increase by 25–30% over the next 25 years [4].

### 1. Parkinson's Disease Risk Factors:

Although a primary cause for Parkinson's disease is yet to be identified, a number of risk factors are clearly evident.

**Advancing age-** Although there is the occasional case of the disease being developed as a young adult, it generally manifests itself in the middle to late years of life. The risk continues to increase the older one gets. Some researchers assume that people with Parkinson's have neural damage from genetic or environmental factors that get worse as they age.

**Sex-** Males are more likely to get Parkinson's than females. Possible reasons for this may be that males have greater exposure to other risk factors such as toxin exposure or head trauma. It has been theorised that oestrogen may have neuro-protective effects. Or, in the case of genetic predisposition, a gene predisposing someone to Parkinson's may be linked to the X chromosome.

**Family history-** Having one or more close relatives with the disease increases the likelihood that you will get it, but to a minimal degree. This lends support to the idea that there is a genetic link in developing Parkinson's.

**Declining oestrogen levels-** Post menopausal who do not use hormone replacement therapy are at greater risk, as are those who have had hysterectomies.

**Agricultural work-** Exposure to an environmental toxin such as a pesticide or herbicide puts you at greater risk. Some of these toxins inhibit dopamine production and promote free radical damage. Those involved in farming and are therefore exposed to such toxins have a greater prevalence of Parkinson's symptoms.

**Genetic factors-** A Mayo Clinic led international study revealed that the gene alpha-synuclein may play a role in the likelihood of developing the disease. Studies showed that individuals with a more active gene had a 1.5 times greater risk of developing Parkinson's. These findings support the development of alpha-synuclein suppressing therapies, which may in the long run slow or even halt the disease.

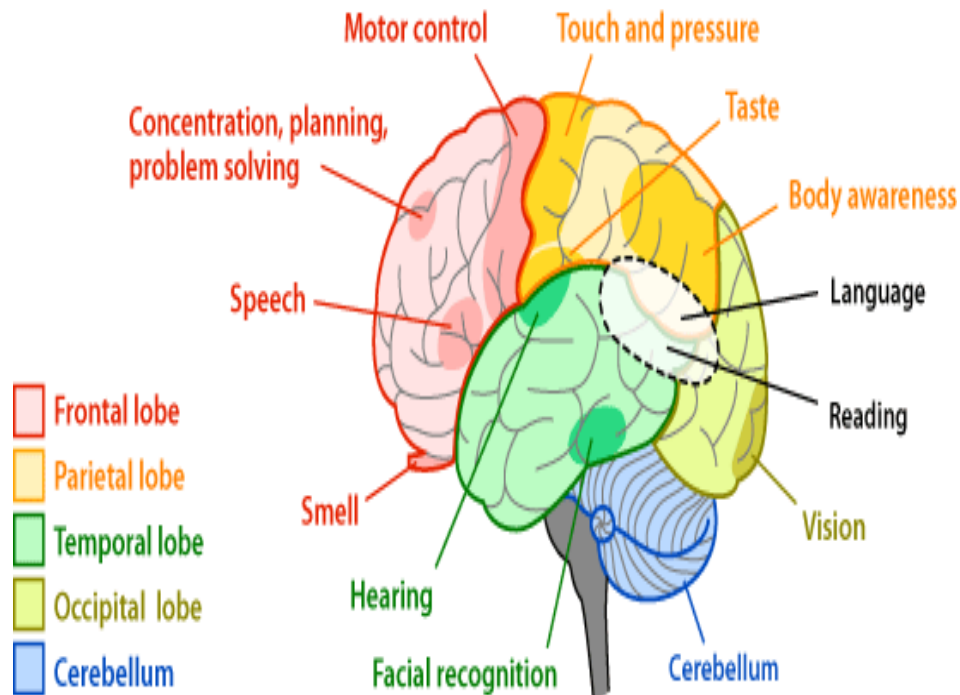
**Low levels of B vitamin folate-** Researchers discovered that mice with a deficiency of this vitamin developed severe Parkinson's symptoms, while those with normal levels did not.

**Head Trauma-** Recent research points to a link between damage to the head, neck, or upper cervical spine and Parkinson's. A 2007 study of 60 patients showed that all of them showed evidence of trauma induced upper cervical damage. Some patients remembered a specific incident, others did not. In some cases Parkinson's symptoms took decades to appear.

Parkinson's Disease is a rare and curious phenomenon, affecting approximately 1 in 300 people. Risk factors mentioned above influence its likelihood to only the tiniest of degrees. Most individuals will have one or more of the risk factors above and never experience any of the symptoms. The one risk factor we all possess is aging, which is a condition that is currently incurable! However, more and more is becoming understood as to how and why these various risk factors influence likelihood of Parkinson's. As knowledge grows, so does the possibility of a cure [5].

## **2:-Short information about brain:**

The brain is made by four lobes and by specific fields, that, for e.g., made us see, ear, catch, and so on.... We can see an image of the brain, in the chapter Brain Functions, that will explain you more about it. The brain has two hemispheres, left and right, that control opposite parts, left-right; right-left.(**Figure.2.**)



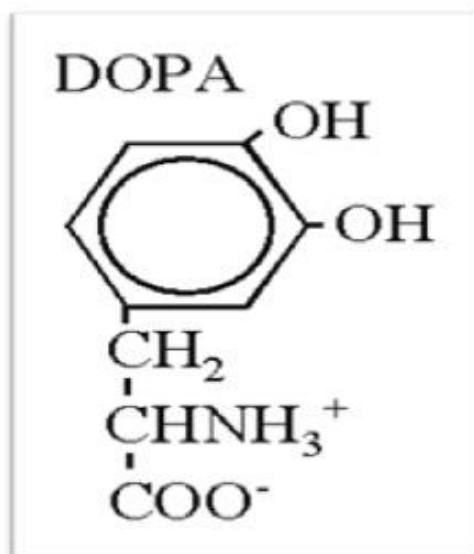
**(Figure.2.Brain)**

**The brain is constituted, himself, by neurons. In the "ramification" of the brain the spinal cord, we have the nerves. We will begin from the neurons that represent the structural unit of the nervous system [6].**

When a person initiates a movement, information from the senses, from parts of the brain that control planning, and from other brain regions travels to a region called the striatum. The striatum then interacts with other areas of the brain — the substantia nigra, globus pallidus, and thalamus — to send out signals that control balance and coordination. These signals travel to the cerebellum, which controls muscle coordination, and then finally down the spinal cord to peripheral nerves in the limbs, head, and torso, where they control the muscles. The molecules that carry information through the brain and spinal cord are called neurotransmitters. Neurotransmitters are special chemicals produced by neurons that accumulate in tiny sacs at the end of nerve fibers. When stimulated, these sacs release neurotransmitters into the gap between neurons, called a synapse. The neurotransmitters cross the synapse and attach to proteins called receptors on the neighboring cell. These signals change the properties of the receiving cell. If the receiving cell is also a neuron, it will carry the signal on to the next cell. If the receiving cell is a muscle fiber, it will react to the stimulation by contracting, which creates movement [7].

**3. Biochemistry of Parkinson disease:**

Parkinson disease is caused by a shortage of a particular chemical that is produced in the brain. This chemical is called dopamine (**Figure.3.**). Without this chemical messenger the signals from the brain do not get through to the spinal cord thence to the various muscles of the body and muscular function is impaired.

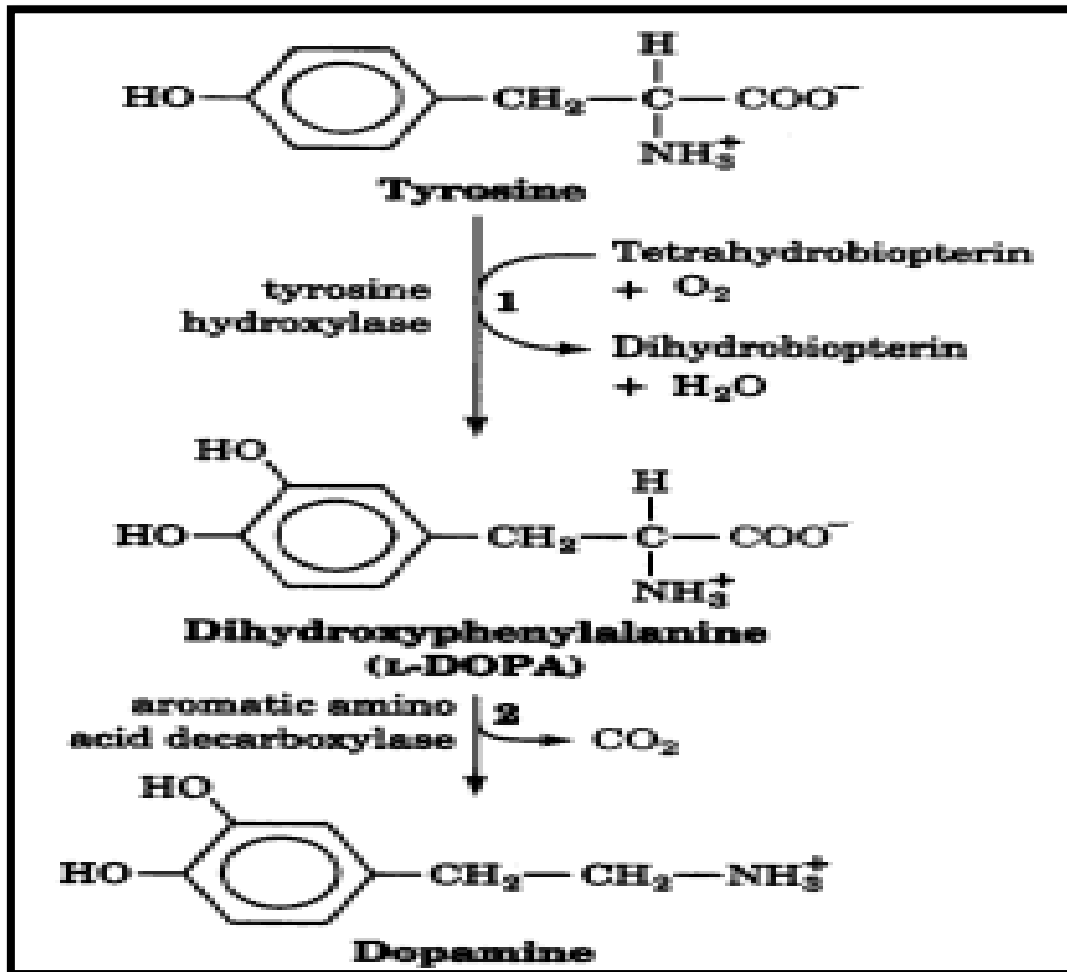


(Figure.3.dopamine structure)

Dopamine is synthesized within nerve cells. Chemically, L-tyrosine is converted to dihydroxyphenylalanine (L-DOPA) and then to dopamine in a two-step process.

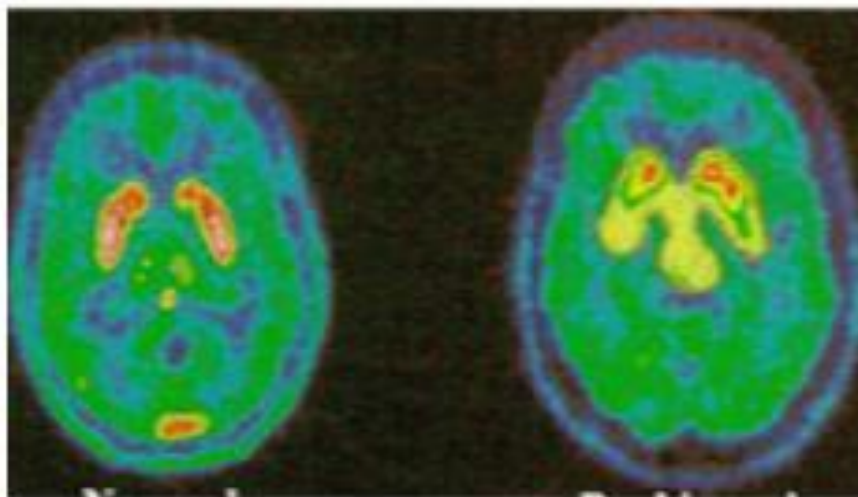
The first, rate limiting step is catalyzed by tyrosine 3-monoxygenase (tyrosine hydroxylase or TH).

The second step is catalyzed by aromatic L-amino acid decarboxylase (L-DOPA decarboxylase).



(Figure.4.Dopamine synthesis)

In parts of the nervous system that release dopamine as a neurotransmitter (dopaminergic neurons) no further metabolism occurs and dopamine is stored in vesicles in the presynaptic nerve terminals. The following image shows the uptake and storage of L-DOPA in human brain, in both a patient with Parkinson disease and a healthy person. The areas have the most uptake. (Figure.4.)



healthy person. The areas have the most uptake. (Figure.4.)

**(Figure.5.)**

Parkinson disease is normally treated by giving patient's L-DOPA preparations in pill form, to replace the dopamine that is missing. Combinations of L-DOPA with other drugs are often more effective.

For example, inhibition of L-DOPA decarboxylase outside of the brain, in the blood stream, allows L-DOPA's effect on the brain to be longer lasting and lessens the "on/off" effects that often accompany medication.

L-DOPA is currently the most effective therapy for Parkinson disease. However, L-DOPA only helps with symptoms and does not prevent the disease from progressing. While it is hoped neurotransplantation with stem cells will provide longer last therapy, this approach is also symptomatic, providing dopamine in a different way. For reasons that are not clear, L-DOPA has side effects which increase over time. Eventually, in advanced disease, the side effects of L-DOPA may outweigh the benefits. In the early stages of disease, dopamine agonists, chemicals that mimic some of the effects of dopamine in the brain are effective [8].

**4. SYMPTOMS:**

**Tremors**- the most noticeable early symptom. It often begins very localised, such as in a finger of one hand. Over time it spreads throughout the whole arm. Tremors often occur when the limb is at rest or when held in a stiff, unsupported position. Tremors also may occur in the lips, feet or tongue.



**Bradykinesia**- slowness of motion. The individual's movements become increasingly slow and over time muscles may randomly "freeze". **Akinesia**- muscle rigidity. Often begins in the legs and neck. These muscles become very stiff. When it affects the muscles of the face the individual adopts a mask like stare. The symptoms of Parkinson's and the rate of progression differ among individuals. Early symptoms of this disease are subtle and occur gradually. For example, people may feel mild tremors

or have difficulty getting out of a chair. They may notice that they speak too softly, or that their handwriting is slow and looks cramped or small. Friends or family members may be the first to notice changes in someone with early Parkinson's. They may see that the person's face lacks expression and animation, or that the person does not move an arm or leg normally.

People with Parkinson's disease often develop a parkinsonian gait that includes a tendency to lean forward; take small, quick steps; and reduce swinging their arms. They also may have trouble initiating or continuing movement.

Symptoms often begin on one side of the body or even in one limb on one side of the body. As the disease progresses, it eventually affects both sides. However, the symptoms may still be more severe on one side than on the other.

Many people with Parkinson's disease note that prior to experiencing stiffness and tremor, they had sleep problems, constipation, loss of smell, and restless legs. While some of these symptoms may also occur with normal aging, talk with your doctor if these symptoms worsen or begin to interfere with daily living.

**Digestion problems-** the ability to process food slows down, resulting in low energy and constipation.

**Depression-** Parkinson's causes chemical changes in the brain that may result in depression. This can be an early warning sign, but as depression becomes more common in older adults, it is not often associated with the disease.

**Low Blood Pressure-** can result in light headedness and fainting.

**Temperature sensitivity-** perception of temperature can be affected, and may result in hot flashes and excessive sweating.

**Leg discomfort-** some patients report burning sensations and cramp in the legs.

**Balance-** There is a progressive loss of coordination and sense of balance, putting the individual at risk of falls [9].

Other symptoms may include:

- Confusion
- Dementia
- Depression
- Memory loss [1].

## 5. How is Parkinson's disease diagnosed?

An early and accurate diagnosis of Parkinson's disease is important in developing good treatment strategies to maintain a high quality of life for as long as possible. However, there is no test to diagnose Parkinson's disease with certainty (except after the individual has passed away). A diagnosis of Parkinson's disease - especially in the early phase - can be challenging due to similarities to related movement disorders and other conditions with Parkinson-like symptoms. Individuals may sometimes be misdiagnosed as having another disorder, and sometimes individuals with Parkinson-like symptoms may be inaccurately diagnosed as having Parkinson's disease. It is therefore important to re-evaluate

individuals in the early phase on a regular basis to rule out other conditions that may be responsible for the symptoms.

A neurologist who specializes in movement disorders will be able to make the most accurate diagnosis. An initial assessment is made based on medical history, a neurological exam, and the symptoms present. For the medical history, it is important to know whether other family members have Parkinson's disease, what types of medication have been or are being taken, and whether there was exposure to toxins or repeated head trauma in the past. A neurological exam may include an evaluation of coordination, walking, and fine motor tasks involving the hands.

The diagnosis of Parkinson's disease is more likely if:

at least two of the three major symptoms are present (tremor at rest, muscle rigidity, and slowness); the onset of symptoms started on one side of the body, symptoms are not due to secondary causes such as medication or strokes in the area controlling movement [10].

## 6. How to prevent Parkinson's disease:

There is no known way to prevent Parkinson's disease.

Research has shown that people who eat more fruits and vegetables, high-fiber foods, fish, and omega-3 rich oils (sometimes known as the Mediterranean diet) and who eat less red meat and dairy may have some protection against Parkinson's disease. But the reason for this is still being studied [11].

## Treatments

### 7. Physiotherapy:

Physiotherapy involves using exercises and other physical strategies to help improve:

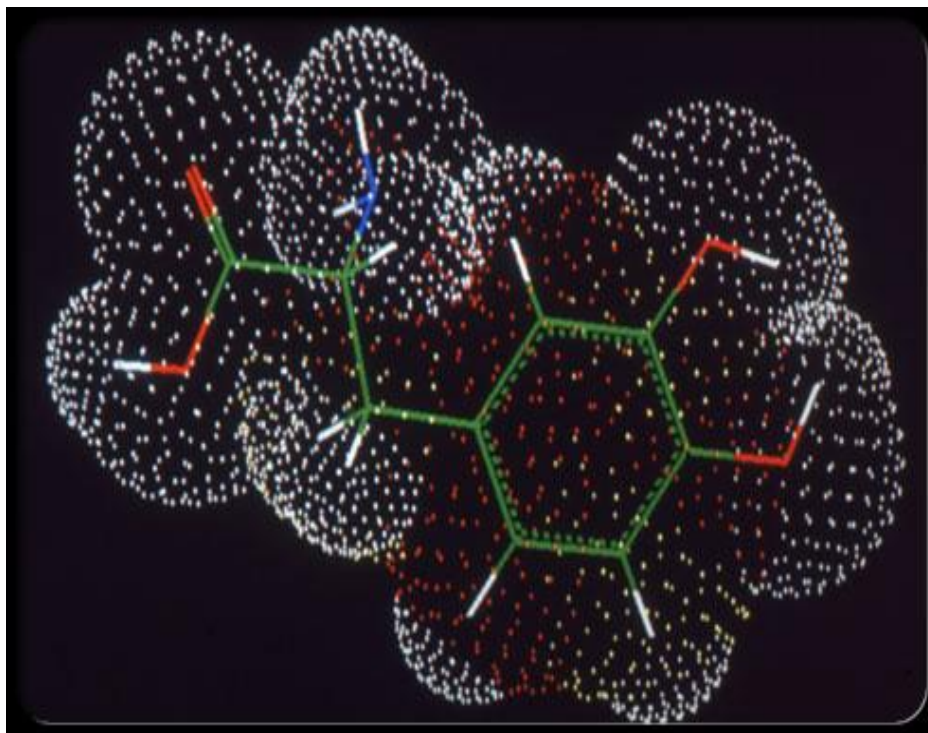
- walking, balance and flexibility
  - aerobic fitness (the sort of exercise that makes your heart and lungs stronger)
  - movement
  - how well you can do things for yourself (for example, how easily you get around, and how well you can carry out everyday tasks). Physiotherapists can also give you advice on staying safe at home.
- A technique called the Alexander technique may be helpful for improving your day-to-day movement [12].

### 8. Medical treatments:

Although there is no cure for Parkinson's Disease, there are several measures that can be taken to improve a patient's quality of life. These measure include drug and surgical therapy. The other options available include making lifestyle changes, and employing physical and speech therapy.

One of the very first options suggested by doctors is medication. There are several drugs available. All with different roles.

- Levodopa – The most commonly prescribed drug for Parkinson's Disease. Levodopa (**Figure.6.**) is a chemical that is able to cross the blood-brain barrier and be converted to dopamine in the brain. It is technically known as a 'precursor to dopamine.'



(Figure.6. Levodopa structure)

- Segeline – It's an MAO-B inhibitor. MAO-B is an enzyme that degrades dopamine, therefore inhibiting this enzyme causes dopamine to have a longer lasting effect on the brain.
- Anticholinergic medications – They block nerve impulses that control muscle movement. They also block acetylcholine, a neurotransmitter that helps to regulate muscle movement. Anticholinergics work best in patients who are over 70, where their main symptoms are tremors and drooling.

Most people manage Parkinson's Disease with medication. But in some cases severe symptoms can heavily reduce one's quality of life and sometimes the medication's side effects are difficult to deal with. In situations like these, a surgical alternative may be sought. There are several surgical options available, these include:

- Pallidotomy – This procedure involves making a lesion in the globus pallidus. That is, destroying some of the cells in a particular part of the brain that controls movement. Pallidotomy has been found to reduce dyskinesias (involuntary movements) by 70%-90%.
- Deep Brain Stimulation (DBS) – Involves implanting a small metal electrode into the brain. The electrode is then attached to a pulse generator which is stored implanted in the chest subcutaneously (under the skin). It is believed that while DBS does not cure Parkinson's Disease, it may diminish drug induced symptoms. A programming device can be used to adjust the pulse generator. This is all done wirelessly. At this stage, only the physician keeps the device which controls the intensity of stimulation. The patient is given a device which determines whether the pace maker is on or off.
- Thalamic stimulation
- Pallidal stimulation
- Subthalamic DBS [13].

## 9. Support for people living with Parkinson's disease

While the progression of Parkinson's is usually slow, eventually a person's daily routines may be affected. Activities such as working, taking care of a home, and participating in social activities with friends may become challenging. Experiencing these changes can be difficult, but support groups can help people cope. These groups can provide information, advice, and connections to resources for those living with Parkinson's disease, their families, and caregivers. The organizations listed below can help people find local support groups and other resources in their communities. There are currently no blood or laboratory tests to diagnose non-genetic cases of Parkinson's. Doctors usually diagnose the disease by taking a person's medical history and performing a neurological examination. If symptoms improve after starting to take medication, it's another indicator that the person has Parkinson's.

## 9. CONCLUSION

Parkinson's disease continues to be a pathology of unknown origin that generates a significant social cost for the patients who suffer from it. Although there is still no definitive cure for this disease at present, there are numerous treatments available aimed at reducing the symptomatology of PD, in addition to other therapeutic alternatives that are still under investigation. However, the therapeutic approach to this pathology should include a combination of pharmacological and non-pharmacological strategies to maximize outcomes and improve symptom astrological control in these patients. In our view, the aim of the clinical trials should delay motor complications in later stages that may show long-lasting complications. However, with the rapid rise of the rate of PD incidence worldwide, finding new multi target drugs or therapies without adverse reactions is a huge challenge.

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