GET THE FACTS

PD 101

WITH IHTSHAM UL HAQ, MD, FAAN

PARKINSON'S
Association of Southwest Florida

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ABOUT THIS EBOOK

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UPCOMING PD TALKS

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INTRODUCTION

PD 101

PD 101 is from T**he Parkinson's Association of Southwest Florida's PD TALK** with Dr. Ihtsham Ul Haq on April 21, 2021. The PASWFL holds Zoom and in-person educational **PD Talks** several times a month that present information on medical and health topics related to PD. The presenters are physicians and non-physician health care professionals, as well as experts in fields with related knowledge and relevance to PD. Talks are Free for members of the PASWFL, and there is no charge to become a member. Visit **ParkinsonAssociationSWFL.org** to learn more.

ABOUT IHTSHAM UL HAQ, MD, FAAN

Dr. Haq is **Division Chief of Movement Disorders at the University of Miami Miller School of Medicine**, Associate Director of the Evelyn-McKnight Brain Institute, and holds the Cornfeld-Hurowitz Endowed Chair in Movement Disorders.

Dr. Haq graduated from Columbia University with degrees in Bioengineering and in Philosophy, completed his residency training at Georgetown, and his fellowship training at the University of Florida. He took his current position in 2020, and over the last five years, has grown the movement team at Miami to 9 clinical faculty and more than 50 affiliated staff.

His overall research interest has been in understanding and improving the care of patients with movement disorders, with a focus on technology and brain circuitry, partnering with foundations, industry, and government to bring better treatments to patients. He has published 3 book chapters and 63 peer-reviewed research articles.

UNDERSTANDING PD

A DISEASE OF THE BRAIN

Parkinson's Disease is a **brain disorder that affects multiple aspects of a person's health**. While it is most commonly associated with its impact on movement, it is fundamentally a disease that eventually involves the entire brain. As such, it interferes with **motor control** and also significantly **influences mood, memory, and cognitive function.**

Understanding Parkinson's as a **whole-brain disease** allows for a more comprehensive approach to treatment and care. This includes addressing the physical symptoms, and emotional and cognitive changes that can accompany the disease.

THE COMPLEXITY OF PARKINSON'S DISEASE

Parkinson's Disease is rooted in a complex system within the brain. One of the key structures involved is the **basal ganglia**—a set of interconnected brain regions that play a central role in governing movement. These regions are highly complex and tightly linked, which contributes to the intricate nature of the disease. The purpose of highlighting this system is not to delve into all the details, but to appreciate the complexity and connectivity that make Parkinson's a challenging disorder.

WHAT IS PARKINSON'S DISEASE ON A BIOLOGICAL LEVEL?

To understand this, we can look at a slice of the **midbrain**, a region of the brainstem responsible for regulating basic bodily functions such as breathing, heart rate, and aspects of cognition. A key area within the midbrain is the **Substantia Nigra,** which produces **dopamine—a critical neurotransmitter involved in movement.**

In individuals with Parkinson's Disease, the **substantia nigra visibly deteriorates**. Under microscopic examination, this area, which normally appears dark due to high levels of dopamine-producing neurons, becomes significantly lighter. This visible loss reflects the decline in dopamine production.

DECREASED DOPAMINE AND THE APPEARANCE OF SYMPTOMS

Parkinson's Disease, at its core, is a condition **characterized by decreased dopamine production**. Various symptoms of PD stem from this neurotransmitter deficit.

Many of the recognizable symptoms of Parkinson's only emerge after significant damage has already occurred.

BY THE TIME SOMEONE BEGINS TO NOTICE TREMORS OR CHANGES IN WALKING, APPROXIMATELY 60% OF THE DOPAMINE-PRODUCING NEURONS MAY ALREADY BE LOST.

This reflects both a challenge and a hopeful aspect of the disease: the brain is incredibly adaptive. Even with up to 80% damage, many people can still function quite normally.

THE GOAL OF TREATMENT IS NOT TO RESTORE FULL FUNCTION, BUT TO RECOVER ENOUGH DOPAMINE ACTIVITY SO THAT INDIVIDUALS CAN LEAD FULFILLING AND MOSTLY NORMAL LIVES.

EARLY NON-MOTOR SYMPTOMS AND DOPAMINE BANKING

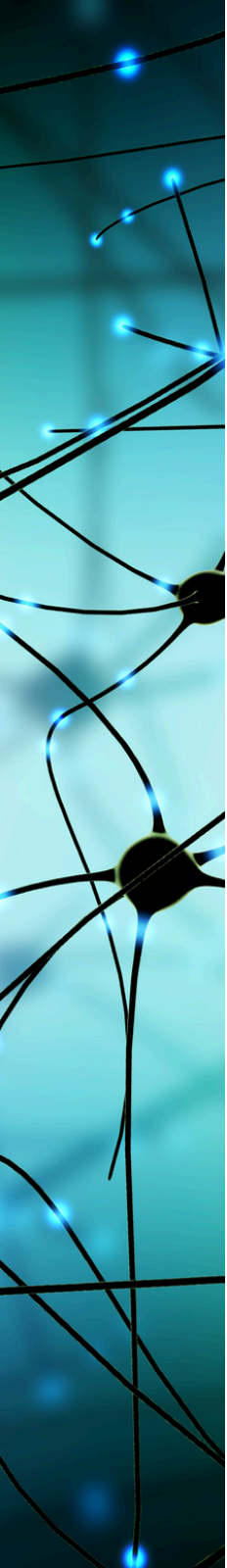
Before the hallmark motor symptoms such as tremors or shuffling gait become noticeable, many individuals with Parkinson's Disease experience **non-motor symptoms**. These early signs can include **changes in sleep patterns, mood disturbances**, and even changes in the **sense of smell**. However, these symptoms are often dismissed or misattributed, as they are not commonly recognized as being linked to Parkinson's.

Many individuals with Parkinson's report experiencing such changes well before a diagnosis is made. These symptoms stem from the same brain changes that eventually lead to movement issues and highlight the importance of early detection and awareness.

Dopamine neurons can be viewed as **'dopamine banks.'** These neurons not only produce dopamine but also store it and release it as needed to coordinate movement. **In Parkinson's Disease, these dopamine banks begin to fail**. The neurons responsible for managing dopamine levels are diminished, and this shortage underlies many of the symptoms experienced.

Understanding the role of these neurons helps lay the groundwork for exploring how medications work—and why they sometimes lead to side effects. These treatments often aim to boost dopamine availability, compensating for the lost storage and regulation capacity of these vital cells.

Dopamine medications don't remain in the bloodstream for long; their lasting effects depend largely on how well the remaining dopamine neurons can store and release dopamine when needed. This underscores the importance of the brain's ability to "hold on" to dopamine as part of effective symptom management.



MOTOR SYMPTOMS

PARKINSON'S AS A DISEASE OF STILLNESS

To better understand how Parkinson's Disease manifests, consider a typical patient. While tremor is often the most widely recognized symptom, Parkinson's is primarily a disease of stillness. Patients may experience **reduced facial expressions**, **slower or more rigid movements**, and a general **decline in motor activity**.

The visual hallmarks of Parkinson's include: a **fixed or mask-like facial expression, reduced hand movement, and a dragging foot**. These features reflect how Parkinson's diminishes a person's ability to initiate and control movement.

Ultimately, the disease reveals itself not in excessive motion, but in the struggle to move—highlighting the core motor deficit that defines Parkinson's Disease.

COMMON MOTOR SYMPTOMS OF PD

Contrary to popular belief, **not all individuals with Parkinson's Disease experience tremors.** In fact, **only about two-thirds of patients present with a tremor,** and many never develop it at all. When present, the **tremor typically starts in one hand and on one side of the body**. This **asymmetrical onset is an important diagnostic clue**. Tremors that begin on both sides simultaneously are generally not characteristic of Parkinson's.

These tremors are called **resting tremors**—they occur when the affected limb is at rest and usually subside during intentional movement. For example, someone may not shake while using a utensil to eat, but might begin to shake again if they hold a fork still for several seconds.

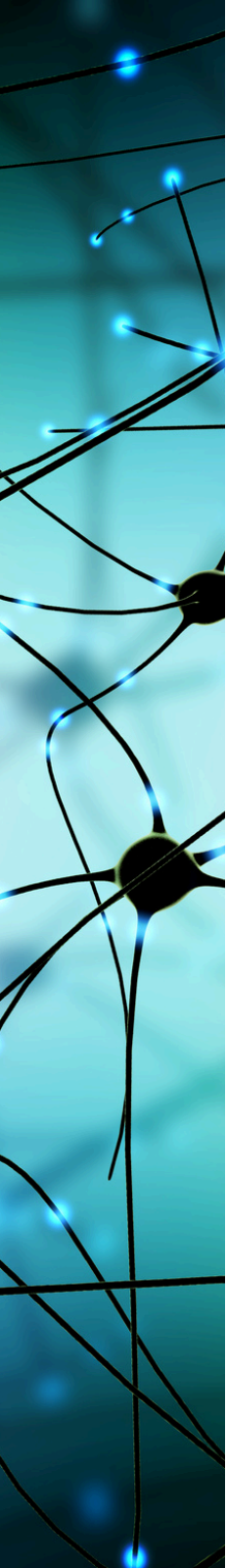
Another prominent symptom is **muscle stiffness**. This rigidity can make limbs harder to move and is often mistaken for simple muscle strain or soreness, especially following physical activity. When this stiffness does not resolve and is accompanied by other symptoms, it may be an early sign of Parkinson's.

Bradykinesia, or slowness of movement, is another core feature. It may affect walking, facial expression, and fine motor skills such as buttoning clothes or writing. Patients often describe difficulty initiating movement, and even rapid eye movements (called **saccades**) can slow down.

Additionally, some individuals experience **balance problems**, particularly as the disease progresses. This can lead to a stooped posture and a distinctive walking pattern known as a **Parkinsonian gait**, characterized by quick, short, shuffling steps.

These motor symptoms—tremor, rigidity, bradykinesia, and balance issues—form the cornerstone of Parkinson's diagnosis and management.

NOT ALL INDIVIDUALS WITH PARKINSON'S DISEASE EXPERIENCE TREMORS



OVERVIEW OF PARKINSON'S DISEASE TREATMENTS

HOW DO WE TREAT PARKINSON'S DISEASE (PD)?

Since the **central problem is the loss of dopamine**, the most effective approach is to **replace dopamine** or mimic its effects in the brain.

AN OVERVIEW OF THE KEY MEDICATIONS USED:

- **Levodopa** – This was the first and remains the most effective medication for Parkinson's. It directly replenishes dopamine levels and is considered the gold standard of treatment.

- **Dopamine imitators** – These medications mimic the effects of dopamine. The main one still used today is **Apomorphine**.

- **Dopamine agonists** – These are commonly prescribed and include brand names such as **Mirapex** (Pramipexole), **Requip** (Ropinirole), and **Neupro** (Rotigotine patch). They act similarly to dopamine in the brain and are especially useful in early or adjunctive treatment.

- **Amantadine** – This medication may be used to manage specific symptoms such as **dyskinesias (involuntary movements),** and still plays a role in treatment for some patients.

MEDICATIONS THAT EXTEND DOPAMINE'S EFFECTS INCLUDE:

- **Entacapone** – helps prolong the effects of Levodopa.
- **Rasagiline** (Azilect) – inhibits dopamine breakdown in the brain.
- **Anticholinergic medications** – Occasionally used to treat tremor, these include **Artane** (Trihexyphenidyl) and **Benztropine**.

While this list introduces the names of medications, we'll delve into their specific uses, mechanisms, and potential side effects in upcoming sections. For individuals living with PD, understanding these treatments can help clarify how to manage symptoms and work with your care team to find the best treatment plan.

CARBIDOPA-LEVODOPA: THE GOLD STANDARD

Developed in the 1960s, **Carbidopa-Levodopa** remains the most effective medication for treating Parkinson's Disease. Levodopa is converted into dopamine in the brain, directly addressing the core issue of dopamine deficiency. **Levodopa** is absorbed in the small intestine via the **large neutral amino acid transporter** (LNAAT). This detail is important because it explains a phenomenon known as the **protein effect**: Levodopa competes with dietary amino acids (from protein) for absorption. If a person consumes a protein-rich meal around the same time as taking their medication, the absorption of Levodopa may be delayed or reduced.

This effect is **generally not a concern in the early stages** of Parkinson's. Early on, the body only needs a small amount of Levodopa to achieve good results. However, as the disease progresses—typically five to ten years after diagnosis—timing medication and meals becomes more important to maximize its effect.

Another common concern is whether long-term use of Levodopa might be harmful to the brain. The idea stems from the fact that dopamine metabolism can generate **reactive oxygen species** (also known as free radicals), which theoretically could damage brain cells. However, current evidence suggests that Levodopa itself does not worsen Parkinson's or cause harm when used appropriately.

There is no need to delay starting Levodopa out of fear of long-term complications. **It remains the most effective tool we have to restore function and improve quality of life for individuals with Parkinson's Disease.**

LEVODOPA REMAINS THE MOST EFFECTIVE TOOL WE HAVE TO RESTORE FUNCTION AND IMPROVE QUALITY OF LIFE FOR INDIVIDUALS WITH PARKINSON'S DISEASE.

PROGRESSION

MOTOR FLUCTUATIONS AND THE PROGRESSION OF PARKINSON'S

Although dopamine metabolism can theoretically create harmful free radicals, this effect is only seen with extremely high doses—levels not used in human treatment but rather in laboratory settings such as animal studies. In clinical use, Levodopa has not been shown to damage the brain.

In fact, some early studies suggested that initiating Levodopa treatment early might even be **neuroprotective**. While subsequent research has not confirmed these findings, it is reassuring that Levodopa neither accelerates the disease nor harms the brain over time. It remains a **symptomatic treatment**—effective for managing symptoms but not altering the disease course. Because it is so central to PD treatment, Levodopa is also a key player in understanding **motor fluctuations**—the changes in how well the medication works as the disease progresses.

In the early stages, Levodopa may work consistently with one to three doses per day. Over time, however, many individuals begin to notice that the medication's effects become shorter-lived. This is primarily due to the **progression of the disease**, not the medication itself.

Remember the concept of dopamine neurons as **banks**. As these banks decline, the brain's ability to store and release dopamine weakens. Levodopa still works—but only for the brief period it is active in the bloodstream. This is why individuals may experience "on/off" states: when the medication is working (on), symptoms improve; when it wears off (off), symptoms return.

Initially, this cycle may occur every five hours. Later in the disease, it might be every two hours or less. This presents a major challenge in PD care: Levodopa still works, but it becomes **less convenient**, requiring more frequent dosing and precise timing.

Delayed on is another fluctuation type. This can happen when Levodopa takes longer to kick in—perhaps 60–90 minutes instead of the usual 30. A common cause is **protein interaction** (as mentioned earlier), but another factor may be **delayed gastric emptying**. Levodopa is not absorbed in the stomach but in the small intestine, so anything that slows stomach emptying can delay medication onset.

Managing these fluctuations is a **critical aspect of long-term Parkinson's care**, and various strategies—ranging from adjusting dose timing to using adjunct medications—are used to help patients regain better symptom control.

DYSKINESIA: WHEN DOPAMINE WORKS TOO WELL

Dyskinesias are involuntary, erratic movements that typically occur when Parkinson's medications, especially Levodopa, are working at their peak. These are not a sign that the medication isn't working—rather, they are a result of **too much dopamine being active at once**.

Dyskinesias often appear as weaving or restless movements of the head, arms, or shoulders. These are not present when the medication is off but are triggered when dopamine levels are high. A helpful way to think about it is that **dopamine unlocks movement**—and dyskinesia happens when too much movement is unlocked at once.

This effect is more common in advanced stages of the disease when the brain's ability to store extra dopamine is greatly reduced. Without enough storage capacity (or "bank"), the dopamine acts immediately—and sometimes excessively—leading to these unintended movements.

People who experience on/off fluctuations are often the same individuals who develop dyskinesias. Managing these symptoms is a balancing act: ensuring enough dopamine to reduce symptoms without tipping over into dyskinesia territory. Later in this book, we'll explore tools and strategies—like medication timing and adjunct therapies—that can help maintain that balance.

DYSKINESIA AND MEDICATION TIMING

As I mentioned earlier, **dyskinesia** occurs during the peak effect of medication. Essentially, it's a result of having too much medication in your system. These extra movements appear when the medication is at its highest concentration. On the other hand, when the medication wears off, you experience the classic Parkinson's symptoms: **tremors**, **stiffness**, and **slowness**.

At first, when you take your medication, it works and **you experience the "on" state**. Sometimes this might lead to dyskinesia, sometimes it won't. However, **over time, you may notice that this "window" of effectiveness becomes shorter**. This is because, unfortunately, as the disease progresses, there are fewer dopamine neurons available to hold onto the medication and release it gradually. Initially, the effects of the medication may last for up to eight or nine hours, but as time passes, this window shortens, typically to about an hour and a half or two hours.

This narrowing of the "on" window is not due to the medication becoming "tolerated" or "stopping" working. Rather, it is a direct **result of the progression of Parkinson's Disease**. **Even if you never took the medication, this change would still occur**, because it's a function of the disease itself. If you were to wait six years to start Levodopa, you would simply begin with a narrower therapeutic window, rather than experiencing the wider window seen in the earlier stages of treatment.

Managing Dyskinesia and Treatment Options

Dyskinesias can be a significant challenge in PD treatment, but the good news is that we have several ways to manage and treat them. However, the onset of dyskinesia is not directly tied to when you start **Levodopa**. It is a process that tends to develop over time as the disease progresses, regardless of when treatment begins.

CARBIDOPA-LEVODOPA: A CRITICAL COMBINATION

You've probably heard me mention **Carbidopa-Levodopa** several times, particularly in the context of **Sinemet**. The reason I use these terms interchangeably is because **Sinemet** is the branded version of **Carbidopa-Levodopa**. When I say **Levodopa**, I'm referring specifically to the dopamine precursor. But why do we pair Levodopa with Carbidopa?

Levodopa is the part of the medication that actually gets converted into dopamine in the brain. However, **Levodopa** also acts on dopamine receptors outside the brain—particularly in the intestines. This can cause **nausea** and other side effects if given on its own. That's where **Carbidopa** comes in. **Carbidopa blocks the peripheral effects of Levodopa**, preventing it from acting in the intestines, where it can cause nausea and vomiting. This is why **Sinemet** is so important.

The **Carbidopa** molecule is large enough that it can't cross the blood-brain barrier, so it only works in the intestines, leaving **Levodopa** free to reach the brain where it's needed. The **25/100** dosage means 25 mg of Carbidopa and 100 mg of Levodopa, which is typically sufficient to prevent nausea without affecting the brain.

DOPAMINE AGONISTS: ANOTHER KEY TREATMENT

In addition to **Levodopa**, **dopamine agonists** are another major class of medications used to treat Parkinson's. These drugs work by mimicking the effects of dopamine in the brain, although they aren't exactly the same as dopamine itself. An example would be **saccharin** compared to sugar: it mimics the sweetness of sugar but is not quite the same thing. Likewise, dopamine agonists can produce similar effects but come with their own set of side effects, which may differ from those of **Levodopa**.

The most common dopamine agonists used in Parkinson's treatment are **Mirapex** (Pramipexole), **Requip** (Ropinirole), and **Neupro** (Rotigotine). These medications are all effective and can be used interchangeably. However, they aren't identical, and the main difference between them lies in their form and how they are administered:

- **Rotigotine (Neupro)** comes as a patch that is applied to the skin and changed daily.
- **Pramipexole (Mirapex)** and **Ropinirole (Requip)** are oral medications, available as pills. These can be taken in a once-daily form, but they're often dosed 2-3 times a day while the doctor works to determine the right dose.

Each of these dopamine agonists has a unique profile of potential side effects, but they can all serve as useful alternatives or complements to **Levodopa** in managing Parkinson's symptoms. If one doesn't work or causes side effects, switching to another may be an option.

Levodopa and Early Treatment: Debunking Myths

There was once a widely-held belief that starting **Levodopa** early in Parkinson's treatment would lead to dyskinesia sooner. As a result, for some time, there was a strong push in the Parkinson's community to prescribe **dopamine agonists**, like **Requip**, **Mirapex**, and **Neupro**, as first-line medications. Some outdated information still lingers, as not everyone has updated their practices. This is often because older medical teachings suggested that using dopamine agonists could help delay or avoid motor complications like dyskinesia. However, recent research has shown that this approach does not prevent dyskinesia from developing.

While **dopamine agonists** have their place and can be helpful, the primary reason for choosing them is often their **side effect profile** rather than their ability to avoid Levodopa. That said, it's important to be aware of these side effects.

COMMON SIDE EFFECTS OF DOPAMINE AGONISTS

1. **Sedation**: Around **30% of patients** may experience **significant sleepiness or drowsiness** on these medications, sometimes leading to **sleep attacks**. It's crucial to be mindful of this, especially if you're doing activities that require alertness, like driving. Always check in with your doctor if you feel excessively sleepy or have trouble staying awake during the day.
2. **Compulsive Behaviors**: This side effect is not common but does occur in about **15%** of patients. It's important to recognize that these behaviors might not be immediately obvious. For example, a person might develop a sudden **gambling habit** or make uncharacteristic financial decisions, like poor purchases or risky stock market investments. These compulsive behaviors can go unnoticed and may seem unrelated to the medication at first.

I have had patients who, after starting **Mirapex** or **Requip**, engaged in behavior they later regretted—such as having affairs or losing money due to gambling. Once these medications were stopped, the behaviors disappeared. The key takeaway here is that **as long as you're aware of the potential for these side effects**, they can be managed. If they do arise, simply discontinuing the medication usually resolves the issue without causing harm.

While not everyone will experience these side effects, it's important to be vigilant. If you're prescribed dopamine agonists or Levodopa, you are taking an effective treatment, and either medication can be a good starting point depending on your symptoms.

THE ADVANTAGE OF DOPAMINE AGONISTS

One significant advantage of **dopamine agonists** is their long duration. Unlike **Levodopa**, which typically needs to be taken at least three times a day, agonists can be taken **once a day** or applied as a **patch** once a day. This is particularly beneficial for individuals who are still working and want to avoid the hassle of constantly keeping track of their medication schedule. With an agonist, you simply take the pill or apply the patch, and you're set for the day.

However, as Parkinson's disease progresses, most people will eventually need both **Levodopa** and a **dopamine agonist**. Levodopa is simply too effective not to use eventually. While agonists are an excellent therapy, **Levodopa** tends to be the backbone of treatment.

LEVADOPA VS. DOPAMINE AGONISTS: KEY CONSIDERATIONS

The decision between **Levodopa** and **dopamine agonists** forms the basis of most treatment plans.

APOMORPHINE: QUICK-ACTING DOPAMINE AGONIST

Apomorphine is a **dopamine agonist** that acts rapidly. It kicks in within about **5 minutes** and lasts for **30 minutes**. Initially, it had to be injected into the thigh, making it more complicated for patients, particularly those with later-stage Parkinson's. However, it's now available as an **under-the-tongue tablet**, which dissolves quickly and is much easier to use. Apomorphine is particularly helpful for people who experience a sudden "wearing off" of their medication.

MEDICATIONS TO ENHANCE LEVODOPA

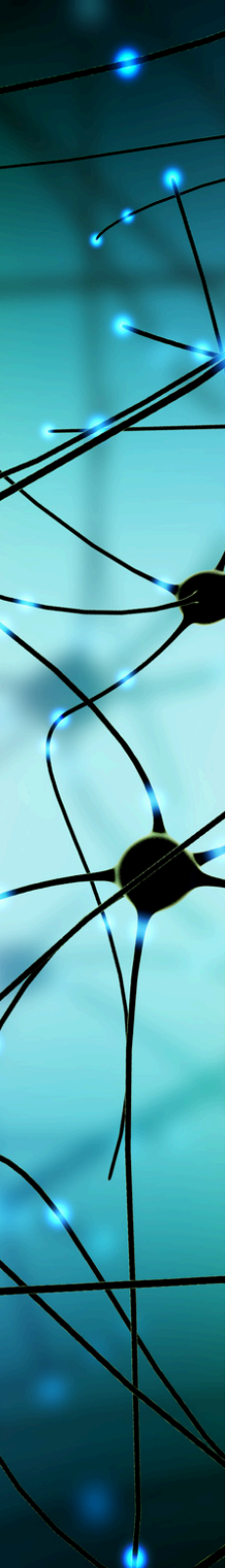
There are also medications that don't directly affect Parkinson's symptoms but help other treatments work better. For example, **Entacapone** is a commonly used medication that doesn't have any effect by itself. Instead, it **slows the breakdown of dopamine**. When taken with **Levodopa**, it makes the effects of Levodopa last longer, which can be particularly useful for patients experiencing "on-off" fluctuations. Another newer medication in this category is **Opicapone**, which is entering trials. It's not necessarily better or worse than Entacapone, it may last longer and could be available soon.

These medications are especially helpful for people with **later-stage Parkinson's** or those whose medication "windows" are shrinking. While these medications can increase dopamine levels, they can also **increase the likelihood of dyskinesia** in patients who are already prone to it. They don't make dyskinesia more likely, but they can push the system past its capacity, leading to more frequent or severe dyskinesia.

RASAGILINE AND LEVODOPA

Rasagiline (brand name **Azilect**) is another medication that helps **extend the effects of Levodopa**. It works through a different mechanism than medications like **Entacapone**. Rasagiline is often used to prolong the activity of dopamine, keeping Levodopa working longer. If you're taking **Azilect**, there's no need for **Comtan** or similar drugs, as you can't "double extend" the effects of Levodopa.

This medication is typically prescribed in the early stages of PD to help patients manage symptoms. By the time most patients see me, their PD has progressed. Early-stage PD patients are often treated well by their primary care doctors. **Azilect** is generally well tolerated with minimal side effects, but like all medications, it can have some unintended effects.



MEDICATIONS FOR COMPLICATED SYMPTOMS

As Parkinson's disease progresses or if complications arise, we may need to consider additional treatments. These medications are usually for **non-dopaminergic symptoms**, like **dystonia** (twisting of the body) or tremor that does not respond to dopamine.
For instance, **dopamine** is excellent at improving **movement**—helping with speed, smoothness, and overall mobility. It also helps with **tremor** in about **75% of people**. However, **25% of patients** don't see improvement in their tremors with dopamine. In such cases, we add other medications, like **Artane** (Trihexyphenidyl), which works well for tremor but does not address stiffness or slowness. It's a **complementary medication**, added to **dopamine therapy** when tremor remains a problem.

BENZTROPINE (COGENTIN)

Benztropine, also known as **Cogentin**, is another medication used in Parkinson's disease, primarily for managing **tremor** and **muscle rigidity** when **dopamine** therapy alone isn't enough. However, it has several **side effects** that can make it less ideal for some patients.

A common **mnemonic** used in medical school to remember its side effects is: **"Can't see, can't spit, can't sweat, can't think."** This refers to:

- **Vision issues** (blurred vision)
- **Dry mouth**
- **Impaired sweating**
- **Cognitive effects**, like confusion or difficulty thinking clearly

These side effects can be **unpleasant**, making Benztropine less favored compared to other Parkinson's treatments. It's typically used only when **dopamine therapy** doesn't address all symptoms.

AMANTADINE

Amantadine is a **weak dopamine agonist** that's primarily used for managing **dyskinesia** (involuntary movements) associated with **Levodopa treatment**. The exact mechanism by which it reduces dyskinesia remains unknown, but it is the only treatment we have that addresses this specific issue once it develops.

Amantadine is also a **weak** medication for other Parkinson's symptoms, like tremor, but it's generally not as effective as **Azilect** for early symptoms.
The **side effects** of Amantadine are also worth noting. **Confusion** can occur, and a specific side effect called **livedo reticularis** may appear. This is a **mottled skin discoloration**, which is more noticeable in the hands and legs.

Here's an example of **livedo reticularis**:

- It can appear after exposure to cold, but when it's due to **Amantadine**, it doesn't go away regardless of weather.
- Over time, if you've been on **Amantadine** for a while, this condition could become permanent.

While **livedo reticularis** is harmless and doesn't pose a serious health risk, it's important to recognize it as a potential side effect of the medication.

AMANTADINE AND ITS SIDE EFFECTS

If you've been taking **Amantadine** for a while, it's important to note that a side effect known as **livedo reticularis** can sometimes become **permanent**. This condition causes a **mottled, bluish skin discoloration**, typically on the hands or legs. While it's **harmless**, it's still important to be aware of this potential side effect.

Amantadine is mainly used **for reducing dyskinesia** (involuntary movements) in Parkinson's disease and doesn't serve much of a purpose for other symptoms.
If you notice **livedo reticularis** while on **Amantadine**, it's probably related to the medication, and it's important to inform your healthcare provider. Again, it's **harmless** but should be monitored.

Non-Motor Symptoms in Parkinson's Disease

Parkinson's disease is not just about the **motor symptoms** (like tremor, stiffness, and slowness). Non-motor symptoms can be just as impactful, and often people don't realize they're experiencing them or may not bring them up, even though they can be very problematic. These symptoms often develop **before the motor symptoms** appear, so they are crucial to address early.

1. Depression

- Depression is **very common** in Parkinson's disease and is often **underrecognized**.
- People with Parkinson's are **more depressed** on average than those with conditions like **stroke** or **multiple sclerosis**, even when those diseases cause more severe symptoms.
- This is because dopamine, the neurotransmitter that's lacking in Parkinson's disease, also helps regulate mood. Without enough dopamine, it's much easier to slip into depression.
- Symptoms of depression in Parkinson's can sometimes be hard to pinpoint because they can be mistaken for other Parkinson's symptoms, like fatigue or memory problems.

2. Fatigue and Lack of Pleasure

- **Fatigue** is common in Parkinson's disease, and it can be a sign of depression.
- Another common issue is the **lack of enjoyment** in daily activities, even things that you used to find pleasurable. This loss of pleasure is a hallmark sign of depression and should not be ignored.

3. Memory and Speech

- **Memory** can also be impacted, both as a result of depression or as a separate issue related to Parkinson's.
- **Speech** is another area affected by Parkinson's. Speech may become **tighter** and **slower**, which happens because Parkinson's affects the muscles used for speaking.

4. Sleep and Tearfulness

- **Sleep disturbances** are common in Parkinson's and can be an early indicator of depression.
- **Tearfulness** without a clear reason is another symptom to look out for. However, **lack of enjoyment** is often the most telling sign of depression in Parkinson's, even when motor symptoms are not severe.

TREATING DEPRESSION IN PARKINSON'S DISEASE

Depression in Parkinson's disease can be treated much like depression in anyone else. The treatments for depression **respond well in Parkinson's patients**. If you notice signs of depression, it's important to bring it up with your doctor to ensure it gets properly treated. Depression can often start **decades before** the motor symptoms of Parkinson's disease appear, so early recognition and treatment are key.

Depression and Apathy:

- It's important to **report symptoms of depression**, **withdrawal, or apathy**, because these are things we can **treat and improve**.
- If activities that once brought you joy are no longer enjoyable, or if you're feeling disconnected from things you used to love, that's something to bring up with your doctor.

Depression, withdrawal, and apathy often overlap, and although they can technically be separate, **they respond to the same treatments**. So, whether you're feeling withdrawn, apathetic, or experiencing sadness, these symptoms can be managed effectively.

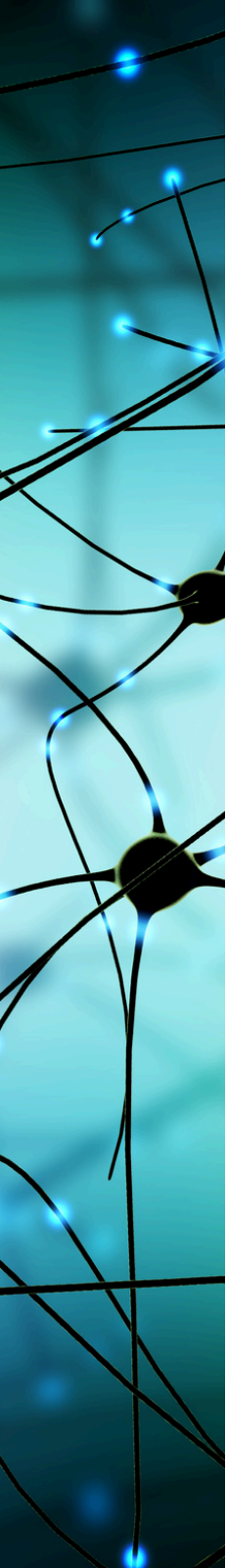
Fatigue:

- **Fatigue** is another common issue for people with Parkinson's. Fatigue is as universal as stiffness and slowness and often arises from a combination of factors:
  - **Muscle stiffness:** If you're stiff, it can be harder to rest, especially at night when turning over in bed becomes difficult, which disrupts sleep.
  - **Effort in daily movements:** Fighting your own muscle rigidity all day takes a lot of energy and leads to fatigue.
  - **Changes in sweating**: Night sweats can also make it tough to rest comfortably.
  - **Sleep disturbances**: Parkinson's disease often causes **REM Behavioral Disorder (RBD)**, where people act out their dreams, sometimes by thrashing in bed, calling out, or even crying out.

- **RBD** affects sleep efficiency. Even if you're technically getting 7-9 hours of sleep, if you're thrashing or calling out, you're not resting well. It might feel like you're getting only **3 hours** of restful sleep.

MANAGING FATIGUE AND SLEEP ISSUES:

- If you're experiencing **REM Behavioral Disorder**, it's essential to **mention it to your healthcare provider**. It's something we can **potentially treat**, and addressing it can lead to better quality sleep.
- **Night-time cramping** and the **short duration of medication effectiveness** through the night can also contribute to fatigue. Since your medication may wear off by the time you sleep, stiffness can persist, and that makes it harder to get good rest.



Addressing Memory Problems in Parkinson's Disease

Memory issues in Parkinson's disease are often **multifactorial** and can be caused by several factors. Unlike some of the other symptoms we've discussed, memory problems in Parkinson's aren't always directly related to the disease itself.

Parkinson's-related memory changes: Typically, people with Parkinson's disease may have trouble with **attention** rather than memory. This can make it harder to recall names or switch topics easily, but **lists** or factual information can still be recalled. If memory issues are more pronounced, it may signal something else.

Other causes of memory issues:

1. **Small strokes**: These are often unnoticed and can contribute to memory problems. They can appear as **white patches** on an MRI, like the one shown here, and are more common in people with conditions like diabetes, high blood pressure, or high cholesterol.
2. **Depression**: This is another common cause of memory issues and can affect both mood and cognitive function.
3. **Alzheimer's Disease**: Unfortunately, it's possible for someone to have both Parkinson's and Alzheimer's, which complicates memory symptoms.

Hallucinations: If memory issues are accompanied by hallucinations, it could be a sign that Parkinson's disease is progressing into a different phase, which warrants further attention.

THE CONNECTION TO VASCULAR HEALTH:

1. **The same factors that affect your heart**—like high blood pressure and high cholesterol—can damage the brain as well. This is why controlling these factors is crucial for brain health.
2. **Exercise** plays a key role in improving both physical and cognitive health, including memory and mood. Regular physical activity is one of the most effective ways to combat cognitive decline, even in those with Parkinson's disease.

While it's important to consider **medication side effects** as a potential cause of memory changes, the key takeaway here is that **exercise** and managing vascular risk factors can have a significant impact on brain health. By maintaining good cardiovascular health, you can reduce the likelihood of memory issues, even if Parkinson's disease is already present.

EXERCISE OFFERS MULTIPLE BENEFITS FOR INDIVIDUALS WITH PARKINSON'S, INCLUDING IMPROVEMENTS IN MEMORY, MOOD, AND OVERALL BRAIN FUNCTION.

CITATIONS:

Parkinson's Association Southwest Florida. "PD 101 - Presented by Ihtsham Haq, MD (Chief, Movement Disorders Division University of Miami Health Systems" Parkinson's Association of Southwest Florida, Parkinson's Association of Southwest Florida, 21 Apr. 2021, https://parkinsonassociationswfl.org/recordings.html

CONCLUSION

You're Not Alone — The Parkinson's Association of Southwest Florida is Here for You

Living with Parkinson's can feel overwhelming, but you don't have to navigate it alone. **The Parkinson's Association of Southwest Florida** is here to support you every step of the way with educational talks, movement and speech classes, wellness programs, and support and social groups that help you live well with PD.

Take the **next step in your journey—sign up for our newsletter and become a member today**. Together, we can help you live your best life with Parkinson's.

STAY CONNECTED AND INFORMED ABOUT PD

A full recording of this PD talk is available at
ParkinsonAssociationSWFL.org/recordings

Sign up to receive a free e-newsletter
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ParkinsonAssociationSWFL.org

To use a QR code, open the camera app on your smartphone and point it at the code. A notification or link will appear on your screen —tap it to be directed to the website or content linked to the code. No special app is needed.

OUR MISSION:
We enrich the quality of life and empower people touched by Parkinson's and related neurodegenerative diseases through exceptional programs and services.

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