Patient's Story

When time pauses, medicine listens: The story of parkinson's disease

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Abstract

Background: Parkinson's disease is one such story — not just of neurons and neurotransmitters, but of people navigating time, identity, and change. To understand it fully, we must move beyond prescriptions and protocols and listen to the lives unfolding within them.

Key words: Parkinson's disease; Neurotransmitters; Awakenings

Medicine often measures success in numbers — improved scores, controlled symptoms, prolonged survival.

But some of its most meaningful moments are quieter.

- A hand that moves again.
- A voice that returns after years of silence.
- A life that continues, even as the body begins to slow.

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Fig (1): Overview of Parkinson's disease—from patient experience to evolving therapies.

1. "Awakenings": When Time Stood Still — and Moved Again

I recently came across Awakenings by Oliver Sacks, and it left me profoundly inspired. He was not just a neurologist, but a storyteller and a humanist — someone who saw beyond disease, into the lives quietly unfolding within it. Where medicine often speaks in terms of symptoms and diagnoses, Sacks chose to tell stories — of courage, consciousness, and identity.

His work takes us back to patients who survived the encephalitis lethargica epidemic of the early twentieth century. They were not asleep, yet not fully awake — suspended somewhere between presence and absence. For years, even decades, they remained in frozen, motionless states, as though time had simply stopped for them while the rest of the world moved on.

They would sit there for hours — unmoving, unblinking — as if time itself had forgotten them. Not asleep, not unconscious, but "present, yet not present."

They were, in his words, "like statues, or figures in a photograph," held in a moment that never seemed to pass. Nurses cared for them, families stayed beside them, but something essential was missing — movement, response, spontaneity. They were seen but not reached.

Then came Levodopa.

What followed felt almost unreal. Patients who had not spoken in decades began to talk. One asked for a newspaper. Another stood up and walked, as if waking from a long, deep sleep. It was not merely clinical improvement — it was an awakening, a return to life itself.

But what made these moments extraordinary was not just movement.

It was the return of presence.

The face was recognized. A voice was answered. People who had long seemed distant turned, however briefly, toward those who had never left their side. For families, these were not medical outcomes — they were reunions. Years of silence were replaced, even if only for a while, by something deeply human: connection.

Yet, the awakening was never simple. For some, it was overwhelming — a sudden release into a world that felt "too fast, too bright." For others, it faded as quietly as it had come, leaving behind a stillness that now carried the memory of what had once returned.

And in that, Sacks learned something essential.

Treating these patients requires far more than a drug. Levodopa could open a door, but it could not hold it open. What remained constant was his presence — the long, patient relationship he built with them and their families. In those relationships lay another kind of healing, one did not measure in doses or duration, but in understanding, patience, and care.

Thanks to these stories, Parkinson's disease became no longer just a neurological condition. It became something deeply human being, a reminder of how fragile and precious the balance of the brain truly is, and how closely it is tied to our ability to exist with others.

Awakenings leave us with more than scientific insight. It reminds us that medicine is not only about restoring function, but about recognizing the person within the illness. As Sacks wrote, to truly understand, we must move beyond case histories and enter stories — where healing is not always permanent, but meaning always remains.

2. From Stillness to a Life in Motion

The awakenings described by Oliver Sacks were brief.

They showed that even after years of silence and stillness, a person could return — speak, move, respond — even if only for a short time. It made one thing clear: the disease may slow the body, but it does not take away the person completely.

Years later, this understanding appeared again — but in a very different setting.

Not in a ward, but in a life that was already in motion.

When Michael J. Fox first noticed a small tremor in his finger in 1991, he was in the middle of a successful acting career. He had already gained worldwide recognition through roles in television and films like Back to the Future. At that stage of life, nothing suggested that his movement — something so essential to his work — would begin to change.

But the tremor remained.

A neurological evaluation confirmed the diagnosis: Parkinson's disease, at the age of 29.

For the next few years, he did what many patients do.

He continued.

He continued acting, working, building his career, and living his personal life — while quietly adjusting to the changes in his body. The disease was present, but not yet visible to the world.

But Parkinson's disease does not stay hidden.

Gradually, the tremor became more noticeable. Movements were not as smooth as before. These were not sudden changes, but steady ones — enough that they could no longer be ignored.

At that point, he made a decision.

He chose to speak openly about his condition.

This moment changed how many people saw Parkinson's disease.

Until then, it was often thought of as a condition affecting only older individuals, something distant from everyday attention. But now, people saw someone young, active, and well-known living with it.

They could see the tremor. They could see the difficulty in movement.

They could see that life was continuing.

He did not step away after that.

He continued acting for several years, including his role in Spin City, even after making his diagnosis public. When symptoms progressed further, he stepped back from full-time acting — not as an end, but as a shift in focus.

In 2000, he established the Michael J. Fox Foundation for Parkinson's Research.

What began as a personal condition became something larger — a structured effort to support research, improve treatment, and bring attention to Parkinson's disease. Over time, this effort contributed significantly to global research funding and awareness.

Even after stepping away from full-time roles, he returned to acting in selected performances, choosing roles where his symptoms did not need to be hidden. In doing so, he showed something important — that the disease does not require a person to disappear from life.

He also spoke and wrote openly about his experience, not to simplify the disease, but to describe it as it is — ongoing, changing, and part of daily life.

In many ways, this was another kind of awakening.

Not the sudden return of movement seen with levodopa,

but a steady, visible continuation of life with the disease.

Just as those earlier patients showed that a person remains present within stillness, this showed that a person continues to live, work, and contribute — even as the disease progresses.

And because it was seen, repeatedly and clearly, Parkinson's disease was no longer something distant.

It became understood.

3. Beyond Medication: The Role of Non-Pharmacological Care

While earlier sections highlight the human experience of Parkinson's disease, management extends beyond pharmacological therapy, particularly as the disease progresses and treatment responses become variable.

3.1. Early and Continuous Supportive Therapies

Non-pharmacological care begins early and continues throughout the disease course.

- Exercise & Physiotherapy- Improves gait, balance, flexibility, and independence→ Requires consistency; benefits decline if stopped
- Physical Therapy- Focuses on gait training, balance, strength, and cueing strategies→ Reduces fall risk and preserves mobility
- Occupational Therapy- Helps maintain independence in daily activities→ Uses adaptive techniques and assistive devices
- Speech & Language Therapy

Addresses:

- Reduced voice (hypophonia)
- Speech clarity (dysarthria)
- Swallowing safety (dysphagia)
- Virtual Reality Rehabilitation (emerging) → Improves balance, gait, and dual-task performance

4. Role in Moderate Disease

As the disease progresses, the focus shifts from improvement → preservation.

- Maintain functional independence
- Reduce falls and complications
- Support communication and nutrition

Therapies become essential to sustain quality of life rather than restore lost function.

5. Surgical Interventions in Advanced Disease

For patients with persistent motor symptoms despite optimised medical therapy, stereotactic neurosurgical approaches are considered to improve quality of life.

- **Deep Brain Stimulation (DBS)**

A stereotactic procedure involving implantation of electrodes into the subthalamic nucleus (STN) or globus pallidus interna (GPi) to modulate abnormal neuronal activity.

DBS:

- Improves tremor, rigidity, and bradykinesia
- Reduces motor fluctuations and dyskinesias
- Allows reduction in medication requirements
- Is adjustable, reversible, and effective for bilateral symptoms

These benefits are most pronounced in patients who demonstrate a good response to levodopa, reinforcing the importance of appropriate patient selection.

- **Stereotactic Neuroablative Procedures**

These procedures involve precise targeting of specific brain regions to alleviate symptoms and are considered when DBS is not suitable.

- Thalamotomy – effective primarily for tremor
- Pallidotomy – improves motor symptoms and levodopa-induced dyskinesia
- Subthalamotomy – reduces motor fluctuations
- MRI-guided focused ultrasound (MRgFUS) – a non-invasive stereotactic technique providing real-time lesioning without surgical incisions

These approaches are typically performed unilaterally due to increased risk of speech and gait complications with bilateral procedures.

6. Patient Selection and Preoperative Considerations

The success of stereotactic surgical interventions depends largely on careful patient selection.

Candidates are typically those with:

- Disabling motor symptoms despite optimal medical therapy
- A clear and sustained response to levodopa
- Sufficient disease duration to confirm idiopathic Parkinson's disease and exclude atypical causes

Comprehensive preoperative evaluation includes:

- Neuroimaging to exclude structural abnormalities
- Neuropsychological assessment to ensure preserved cognition
- Psychiatric evaluation for mood and behavioural stability

- General medical assessment for surgical fitness

Equally important are patient expectations, social support, and the ability to participate in postoperative care.

Surgery is not curative. Patients must be counseled that the goal is improvement in quality of life, with continued disease progression and the likelihood of ongoing need for pharmacological therapy.

A multidisciplinary team approach remains essential for optimal outcomes.

7. Emerging and Investigational Approaches

- **Neural Transplantation**

Therapies involving transplantation of dopamine-producing cells aim to restore dopaminergic deficits. While conceptually promising, clinical trials have shown inconsistent benefits, with challenges related to graft survival, dyskinesia, and disease involvement in transplanted cells limiting current application.

- **Gene Therapy**

Gene-based approaches aim to enhance dopamine production, modulate neural circuits, and protect neuronal function. Early studies have demonstrated safety, though consistent clinical efficacy and long-term benefits remain under investigation.

8. Evolution of Pharmacological Management in Parkinson's Disease

While non-pharmacological strategies strive to preserve function and independence, the journey of Parkinson's disease is equally defined by the evolution of pharmacological therapy — an ongoing effort to restore what the disease gradually takes away.

From early symptomatic relief to dopamine replacement and emerging disease-modifying approaches, pharmacological management has transformed Parkinson's disease from a condition of helpless progression to one where meaningful symptom control is possible.

Parkinson's disease (PD), first described by James Parkinson in 1817, has seen remarkable progress in its pharmacological management. From rudimentary symptom palliation to cutting-edge disease-modifying therapies, antiparkinson drugs have transformed patient lives. This article traces their development year by year, highlighting mechanisms, breakthroughs, and future directions as of March 2026.

8.1. Foundations: 1817–1950s

The journey began with James Parkinson's seminal 1817 essay, "An Essay on the Shaking Palsy," detailing resting tremor, rigidity, bradykinesia, and postural instability. Without understanding dopamine's role, early treatments focused on symptom relief.

Pre-1950s therapies centered on anticholinergics like belladonna alkaloids (hyoscyamine) and synthetics such as trihexyphenidyl. These blocked excess acetylcholine in the

striatum to counter dopamine loss, primarily easing tremor (50–70% efficacy) but offering limited bradykinesia control. Side effects—dry mouth, constipation, and confusion—restricted use, especially in older patients. Surgical options like thalamotomy provided temporary relief but carried high risks.

8.2. Dawn of Dopamine: 1910s–1960s

Levodopa (L-DOPA), the dopamine precursor, was synthesised in 1911 by Casimir Funk, but therapeutic potential emerged later. By the 1960s, researchers recognised that substantia nigra neuron loss depletes striatal dopamine.

1967 marked the revolution: George Cotzias administered high-dose levodopa, which crosses the blood-brain barrier (1–5%) and converts to dopamine via DOPA decarboxylase (AADC), replenishing striatal terminals to directly reverse bradykinesia/rigidity (70–80% response). Patients experienced dramatic motor improvements, shifting PD care from palliation to restoration.

8.3. Refinements and Adjuncts: 1970s

1970: Carbidopa, a peripheral AADC inhibitor, combined with levodopa (Sinemet), minimised nausea and wasting by enabling brain-specific conversion. Blocks extracerebral L-DOPA metabolism (75–80% dose reduction), boosting central dopamine without peripheral side effects like hypotension. Doses stabilised at 150–1000 mg/day levodopa equivalent.

1973: Amantadine, initially an antiviral, gained approval for its mild NMDA antagonism, aiding early symptoms and later dyskinesias.

1979: Selegiline, the first MAO-B inhibitor, blocked dopamine breakdown (extends half-life 40–60%), suitable for monotherapy in early PD or adjunctively.

8.4. Agonist Era: 1980s–1990s

1980s: Bromocriptine, an ergot-derived D2 agonist, directly stimulates postsynaptic D2 receptors in the striatum, mimicking dopamine for levodopa-sparing effect (20–30% less potent), delaying motor fluctuations but with fibrosis risks.

1991: Pergolide (another ergot agonist). Broad D1/D2 agonism for balanced direct/indirect pathway activation; later withdrawn for cardiac valvulopathy.

1997: Safer non-ergot agonists pramipexole and ropinirole targeted D2/D3 receptors, preferentially activating the direct pathway, improving bradykinesia; ideal for young-onset PD but linked to impulse control disorders in 15–20% via mesolimbic effects.

1998: Entacapone, a COMT inhibitor. Blocks catechol-O-methyltransferase, preventing peripheral levodopa breakdown to 3-OMD (boosts AUC 25–50%, extends on-time). Tolcapone (1997) adds central inhibition, but restricted due to hepatotoxicity.

8.5. Advanced Delivery: 2000s

2004: Subcutaneous apomorphine (Apokyn). Potent non-ergot D1/D2 agonist for rapid rescue (15-min onset); continuous infusion stabilizes receptor stimulation during off-periods.

2006: Rasagiline, an improved MAO-B inhibitor, Selective, irreversible MAO-B blockade (like selegiline but cleaner profile); ADAGIO trial hinted at neuroprotection via reduced oxidative stress.

2007: Rotigotine transdermal patch. Continuous D1–D3 agonism via skin delivery avoids pulsatile stimulation, ideal for adherence/nighttime symptoms.

2009: Duodopa intestinal gel infusion. Bypasses gastric variability for steady plasma levodopa/carbidopa, minimizing fluctuations in advanced PD.

8.6. Sustained Release Innovations: 2010s

2015: Rytary, an extended-release levodopa/carbidopa. Multimodal beads prolong absorption (3–4x daily vs. 5–6x), smoothing plasma peaks/troughs for stable striatal dopamine.

2016: Opicapone, a once-daily COMT inhibitor. Potent, peripheral COMT blockade (long half-life) extends levodopa duration without daily dosing

2017: Amantadine extended release (Gocovri). Sustained NMDA/glutamate modulation + dopaminergic facilitation cuts dyskinesias 30–40% at bedtime.

2019: Istradefylline. Adenosine A2A antagonist in globus pallidus reduces indirect pathway overactivity, cutting off time without worsening dyskinesia.

8.7. Neuroprotection Horizon: 2020s

2020–2025: Safinamide (2015 EU approval, expanded). MAO-B inhibition + glutamate release inhibition + sodium channel modulation for multifaceted off-time/dyskinesia control.

2023–2024: Repurposed GLP-1 agonists like exenatide and lixisenatide. Activate GLP-1 receptors on dopaminergic neurons, promoting neurotrophic factors, anti-inflammation, and mitochondrial protection to slow progression.

2024: ND0612 subcutaneous levodopa/carbidopa. Continuous SC infusion mimics physiologic dopamine, superior off-time reduction vs. oral.

2025: Tavapadon, a selective D1/D5 agonist, advanced toward approval for smoother symptom control. Adaptive deep brain stimulation (DBS) emerged, real-time, adjusting to brain signals. Targets the direct pathway for dyskinesia-sparing motor control.

2025: Roche's prasinezumab, an anti-alpha-synuclein antibody, entered Phase III. Binds/neutralizes pathogenic aggregates, potentially halting Lewy body spread.

2026 Outlook: Stem cell therapies (bemdaneprocel), c-Abl inhibitors (nilotinib), and gene therapies (ProSavin) near pivotal trials. Biomarkers like DaT-SPECT and CSF alpha-synuclein guide precision medicine.

9. Current Pharmacotherapy options for PD in India

Drug Class	Generic Drugs
Dopamine Precursors	Levodopa/Carbidopa, Levodopa/Benserazide, Levodopa/Carbidopa/Entacapone

Dopamine Agonists	Pramipexole, Ropinirole, Rotigotine, Apomorphine
Ergot Agonists	Bromocriptine, Pergolide
MAO-B Inhibitors	Selegiline, Rasagiline, Safinamide
COMT Inhibitors	Entacapone, Opicapone, Tolcapone
NMDA Antagonists	Amantadine
Anticholinergics	Trihexyphenidyl, Procyclidine, Biperiden, Orphenadrine, Benztropine
PD Psychosis	Pimavanserin

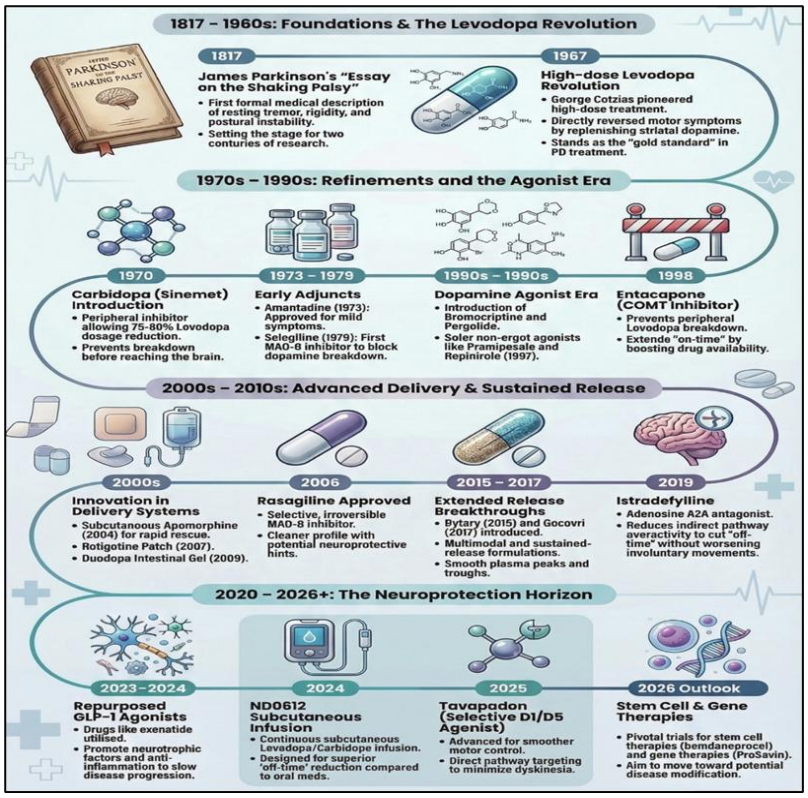

Fig (2): Evolution of pharmacological therapies in Parkinson's disease across major milestones.

10. Conclusion

The Human Side of Healing

Parkinson's disease is often described through what is lost — movement, speed, ease. But these stories remind us of something equally important.

Even in stillness, a person remains; Even in progression, life continues.

From the silent wards of Awakenings to the visible journey of Michael J. Fox, to the evolving science of treatment. One truth remains constant: Medicine is not only about restoring movement. It is about recognizing the person within the disease. Because in the end, the goal is not just to treat Parkinson's disease, but to ensure that no life within it goes unseen.