

Surge.

Not electrical, more visceral than that;
ebbing its way through your bloodstream,
through your irritated vitals, through those
bony fingertips and finishing up at your
heavy frontal lobe where it resides a
while... then, vibrating through synapses
and travelling back down your spinal cord,
you relive it all over again.

Shaking.

Not badly, more like a shudder; a wobble,
a quiver, a tremble, an *oscillation*, sucking
at your senses through straws in dirty
plastic cups.

Your hands don't belong to you anymore.
They're intrusive protrusions leaning
carefully on the borders of being perverse
and safeguarding. Veins popped, prepped
and ready to leap from your thin skin like
they're pulsating, spitting, splitting and
eager to escape from *it*.

There are small pauses and there is an
urgency. They are sensual and they want
to be maintained and kept in this delicious
flux.

When facing an unquantifiable value, the
only position left to take is abject humility.

Parkinson's Disease, Mitophagy, and Dopamine Neurons: Unravelling the Intricate Connection

Parkinson's disease remains an enigmatic challenge in the realm of medical research, as the pursuit of a cure has proven elusive. The plight of scientific researchers is a relentless one, marked by countless hours of dedication and unwavering commitment to unravelling the mysteries of this neurodegenerative disorder. The inability to find a cure underscores the complex nature of the disease, where multiple factors and mechanisms come into play, making it akin to solving a multifaceted puzzle. On top of that, the journey towards a cure is hampered by the prevalence of ignorance toward unseen disabilities, as Parkinson's often manifests with symptoms that aren't immediately visible. The struggle of those living with Parkinson's to convey the daily challenges they face can go unnoticed, reinforcing the need for increased awareness and support for both patients and researchers.

Parkinson's disease (PD) is a complex neurodegenerative disorder that primarily affects the motor system, leading to tremors, rigidity, bradykinesia (slowness of movement), and postural instability. This disease is characterised by the gradual loss of dopamine-producing neurons in a specific region of the brain known as the substantia nigra, which is part of the basal

ganglia. While the exact cause of Parkinson's disease is still not fully understood, researchers have made significant progress in uncovering the role of mitophagy and its relationship with dopamine neurons in the context of the disease.

Mitophagy: A Cellular Cleanup Mechanism

Mitophagy is a vital cellular process that involves the targeted removal of damaged or dysfunctional mitochondria, the energy-producing organelles within cells. This process is essential for maintaining cellular health and preventing the accumulation of dysfunctional mitochondria, which can lead to oxidative stress and cell death. In the context of Parkinson's disease, disruptions in mitophagy have been implicated as a significant contributor to the progression of the disease.

The Role of Mitophagy in Parkinson's Disease

Research has shown that defects in mitophagy pathways can lead to the accumulation of damaged mitochondria within dopamine-producing neurons. As these neurons are particularly vulnerable to oxidative stress due to their high energy demands and dopamine metabolism, the buildup of dysfunctional mitochondria can trigger a cascade of events that contribute to their degeneration. The loss of

dopamine neurons results in reduced dopamine production in the brain, leading to the characteristic motor symptoms of Parkinson's disease.

Dopamine Neurons: Key Players in Motor Control

Dopamine neurons play a critical role in the brain's reward and motor control systems. They are responsible for producing dopamine, a neurotransmitter that transmits signals between nerve cells and is involved in regulating movement, motivation, and emotional responses. In Parkinson's disease, the degeneration of dopamine-producing neurons disrupts the delicate balance of dopamine levels in the brain, leading to the motor impairments that define the disease.

The Interplay Between Dopamine Neurons and Mitophagy

Dopamine neurons are particularly reliant on efficient mitochondrial function due to their high energy demands. When mitophagy is impaired, damaged mitochondria accumulate, compromising energy production and increasing oxidative stress within these neurons. This oxidative stress can lead to the accumulation of toxic protein aggregates, such as alpha-synuclein, a hallmark of Parkinson's disease pathology.

Efficient mitophagy is crucial for maintaining the health of dopamine neurons. Research suggests that dysfunctional mitophagy may contribute to the initiation and progression of Parkinson's disease by promoting neuroinflammation, oxidative stress, and protein misfolding, all of which contribute to the degeneration of dopamine neurons.

Therapeutic Implications and Future Directions

Understanding the intricate connection between Parkinson's disease, mitophagy, and dopamine neurons opens up new avenues for potential therapeutic interventions. Researchers are exploring strategies to enhance mitophagy pathways as a means to prevent or slow the progression of Parkinson's disease. These approaches aim to restore mitochondrial health, reduce oxidative stress, and ultimately protect dopamine neurons from degeneration.

Do you ever find yourself ensnared within the crevices of recommended video content, contemplating the provenance of these productions? Are they crafted by knowledgeable authorities or mere purveyors of unfiltered, uninformed, and fantastical narratives cast into the digital abyss? If I think about the back-end I find it bleak. The sombre reality emerges, where human moderators laboriously delve into the shadowy depths of online content (comments, videos, images, text, sound) in their quest to shield us from the concealed depths of the human psyche, masked by avatarian counterparts or pseudonyms.

Searching YouTube for answers to medical concerns isn't advised.

An innocent enquiry into the long-term effects¹² of trichloroethylene³ (TCE, tricky, trick, tri) on brains exposed to this sweet-smelling colourless liquid leads to a nefarious mix of conspiracy pieces laced with political nefariousness and hyperbolic

¹ Matej, A. (2022) 'Rates of Parkinson's disease are exploding. A common chemical may be to blame,' The Guardian, 10 January. <https://www.theguardian.com/commentisfree/2021/apr/07/rates-of-parkinsons-disease-are-exploding-a-common-chemical-may-be-to-blame>.

² Sullivan, W. (2023) 'Common Chemical Strongly Linked to Parkinson's,' Smithsonian Magazine, 23 May. <https://www.smithsonianmag.com/smart-news/common-chemical-strongly-linked-to-parkinsons-180982216/#:~:text=A%20study%20of%20military%20veterans,is%20linked%20to%20Parkinson's%20disease>.

³ Trichloroethylene is a halocarbon with the formula C₂HCl₃, commonly used as an industrial degreasing solvent. It is a clear, colourless non-flammable liquid with a chloroform-like sweet smell.

news pieces imposing fear and loathing with added celebrity cachet.



Recall the last time you felt exceptionally well and describe your living conditions at that time. Mention any factors, such as the type of residence, age, carpets, heat source, paint, and proximity to industrial areas. Similarly, provide details about your work environment when your health issues began, including the type of building, ventilation, exposure to toxins, and neighbouring businesses.

Have health-related reasons ever prompted you to change your residence or job? Have you experienced a known chemical injury or significant exposure? In

the course of work or schooling, have you been exposed to chemicals or toxic metals, and if so, provide details regarding the nature, duration, and names of these substances? If you've worked near businesses regularly using such substances or in buildings with closed windows, when and for how long did this occur? Were there instances where you or your co-workers complained about air quality, smells, or suffered injuries at your workplace, and when did these occur?

Were there any incidents or concerns about air quality in your place of work? Have you lived near heavy industries emitting waste into the air or water, such as golf courses, dry cleaner plants, shipyards, mines, chemical factories, or dumpsites? Specify the type of pollution, duration, and when these experiences took place.

Describe the use of aerosol sprays, chemicals, cleaners, construction, painting, and the frequency of pesticide or herbicide usage inside or outside your home. Have you lived near busy highways, streets, or gas stations, and when was the last time your air ducts were cleaned or air filters changed?

Have you ever felt your feet stick to the ground? Not actually stuck with glue, but stuck because your muscles aren't sending the right messages to your brain. Stuckness is common; stuckness of the

body, of the postural instability, stuckness of the tremors in the hands and fingers, stuckness of being unable to open jars and packets and wine bottle tops, stuckness of the relentless restless feet with the toes seizing and becoming hard as if they've had metal rods inserted into their tiny bones. Have you ever felt unable to smile, not because you weren't happy, but because you have limitations on the accuracy of emotional expression in the face due to a decrease in the speed and coordination with which the facial musculature is activated?

...the doctor said to me, "you don't win this, you lose."

"I'm not *not* being careful, it's just I have this, this um, illness, this condition, it doesn't recognize, umm, authority. It doesn't recognize my brain saying slow down, it doesn't care."

Is there a poetic significance in the process of getting rid of damaged cells? One might contemplate this with a touch of empathy or anthropomorphism, envisioning these cells earnestly striving to assist, yet inadvertently causing harm to the body. The discernment of this intricate interplay prompts reflections on the nature of Parkinson's Disease (PD) in comparison to other maladies like cancer, where the ailment is distinctly delineated from one's body and psyche, presenting itself as a somewhat separable entity. The alienation that often accompanies a

cancer diagnosis, where the disease is perceived as something to be fought and eradicated, evolves into a more intricate relationship with Parkinson's. Rather than an entity to be battled, Parkinson's becomes a part of the person's identity that they must learn to coexist with. In contrast, PD exhibits a greater complexity, entwined with neurological determinants. Neurological disorders challenge the conventional notion of an indivisible unit or body that defines our identity, disrupting the clear distinction between 'us' and 'it.'

The dissolution of this conceptual boundary compels an acceptance of PD that differs from the rejection of an alien other, as often seen in the case of cancer. Instead, it invites a nuanced approach, akin to seeking harmony with PD and learning to coexist with its less-than-desirable presence, as it becomes an integral part of the person. Navigating life with Parkinson's is akin to finding ways to harmonise with an uninvited guest. Just as a garden might contend with the encroachment of vines like knotweed and buddleia, individuals with Parkinson's strive to find balance between their own aspirations and the challenges posed by their condition. In this analogy, a garden becomes a symbol of resilience and growth amid challenges. Parkinson's, while unwelcome, encourages an exploration of one's own capacity for adaptation and the discovery of new dimensions of self.

The amalgamation of a degenerative disease and one's parent juxtaposes that of the relationship between parent and child; roles reversed and struggled against stubbornly. It's a transformative process but not always transforming - the preservation of longstanding relationships is upheaved, sometimes suddenly other times over a decade or more. One person is lost, the other losing. One person fighting for the return of the past, the other trying to keep everything as it was. Navigation of the complexities brought on by illness is both weird and eerie, allowing us "to see the inside from the perspective of the outside, for that which lies beyond standard perception, cognition and experience."⁴

If "Cruel Optimism"⁵ refers to a situation in which individuals hold onto optimistic beliefs or aspirations that are ultimately unattainable or even detrimental where people find themselves caught in a paradox where their hopes for the future are entangled with conditions that prevent them from realising those hopes. **And if** despite recognising the challenges, they continue to invest in these aspirations, leading to emotional exhaustion, disappointment, and a sense of being trapped in an unsustainable or unhealthy

situation, **then** PD becomes an optimism that is cruel because it sustains a cycle of unfulfilled desires and prevents individuals from moving forward or finding genuine well-being.

Someone once told me that it's mostly dopamine neurons that are lost in people with PD. It made me think that a prolonged period of unhappiness can be terminal.

⁴ Fisher, M. (2016). 'The Weird and the Eerie'. London: Repeater.

⁵ Berlant, L. (2011). 'Cruel Optimism'. Duke University Press.

YouTube's 21 next recommended videos on "trichloroethylene and parkinson's disease":

Understanding Parkinson's disease
Vitamins, supplements, & other drugs for Parkinson's disease... Billy Connolly says life with Parkinson's disease 'has itsThe Long Road to Hope: Ending Parkinson's Disease What's it like to have Parkinson's? Parkinson's UK Alan Alda reveals Parkinson's disease diagnosis Why Does Parkinson's Affect People Differently? Understanding Off Episodes and Dyskinesia in Parkinson's Neuroscience Expo: What Causes Parkinson's Disease? Military Toxic Exposures: What You Need to Know The Long Road to Hope: Ending Parkinson's Disease [FULL Environmental Exposures in Veterans with Parkinson's Why women with Parkinson's are misdiagnosed more often than men A groundbreaking Parkinson's treatment has brought normalcy back to this man's life CBC NL - Newfoundland and Labrador Mid-Stage Parkinson's Disease: Problems with Moving...The Latest Research on Exercise and Parkinson's - THE VICTORY SUMMIT® VIRTUAL EVENT: EXERCISE The Alarming Rise in Parkinson's Disease with Dr. Ray Thinking and Memory Problems with Parkinson Disease Cannabis and Parkinson's Disease Understanding Parkinson's Disease (Including Direct and What is Parkinson's disease? | Nervous system diseases |

NCLEX-RN | Pharmacology - Parkinson's Disease, Levodopa meds nursing RN PN NCLEX Parkinson's Disease (Shaking Palsy) - Clinical Presentation...Why women with Parkinson's are misdiagnosed more often than men...Michael J. Fox on Parkinson's, and maintaining optimism Cannabis and Parkinson's Disease Demystifying Medicine McMaster Parkinson's Disease Symptoms, Treatment, Nursing Care, Pathophysiology NOW PLAYING Understanding Off Episodes and Dyskinesia in Parkinson's DiseaseWhat are the different stages of Parkinson's disease? The Parkinson's You Don't See: Cognitive and Non-motor...The woman who can smell Parkinson's disease...Update on Parkinson's Disease and Parkinson's Syndromes 7 Motor Symptoms of Parkinson's Disease Watch how a device in his chest helps manage his Parkinson's disease The Latest and Greatest in Parkinson Research TWiN 30: Gut to brain spread of alpha-synuclein in Parkinson's Parkinson's disease "What do successful people do to slow down PD progression?" Dr. Laurie Mischley Cognitive and Non-motor Symptoms of Parkinson's Disease Davis Phinney Foundation for Parkinson's New Treatment for Parkinson's Disease Patients - Focused Ultrasound is Safe and Effective...Managing hidden Parkinson's symptoms The ONLY Proven Way to Slow Down Parkinson's What are the symptoms of Parkinson's Disease? Ask the Experts

ButlerHospital...What causes the loss of dopamine neurons in Parkinson's disease? Animated Parkinson's Patient ... How does exercise slow progression in Parkinson's disease?...Reversing Parkinson's Disease With Fast Walking and What the Heck is GDNF?? Exercise and Parkinson's Disease Progression What is Parkinson's Disease? The Michael J. Fox Foundation for Parkinson's Research Parkinson's Disease Exercises: Posture Parkinson's Foundation...Vagus Nerve Activation | Update on Parkinson's Disease and Parkinson's Syndromes Reversing Parkinson's Damage | Science In The Hospital The What and Why of Parkinson's Motor Symptoms - The Victory Summit Event: Motor Symptoms Parkinson's Disease Exercises: Arm Strength Parkinson's Disease Exercises: LSVT LOUD Vocal Therapy Exercise Recommendations for Parkinson's Disease The 5 reasons why are my Parkinson's medications not...Urinary Dysfunction and Parkinson's with Arun Mathur Tips for Better Living with Parkinson's NOW PLAYING This is Parkinson's S1 EP 2...Yoga Therapy for Parkinson's and Anxiety/Depression Parkinson's Disease Exercises: Brain and Body Ep. 10 How Long Have I REALLY Had Parkinson's? Mirjam Holzel speaks about living with Parkinson's Disease Interview with the Authors of Goodbye Parkinson's Hello Life Parkinson's Disease: The Basics Parkinson's

Disease:- Prof Bas Bloem "What type of exercise is best for people with Parkinson's" Sleep and Parkinson's disease with Dr. Ron Postuma...NOW PLAYING ▣



I don't remember much from the day it happened. We weren't expecting it, to be honest, least of all you. We thought it was a trapped nerve in your right arm; you'd always been a gym bunny and incredibly active into your golden years. Lifted a weight too heavy, maybe? Pulled something deep inside that fucked something else up, probably? But not this. You got told in the same hospital outbuilding that grandma went to die. They called it respite, but a "momentary halt in activity" felt spiteful. It was an in-between house except it was without the decades-old furniture and soft mildew smell emanating from the mustard velvet curtains in the front room. It had nothing of her and yet it became her in those final days, hours.

It was depressing to be back ten years later. Walking up those concrete steps into spinach green and early 2000s abstract floral paintings in sickly golden frames. Nothing changes until everything does. I waited outside when they called you in. I'll only be a mo you said, almost festive. Now I know it to be your game face; your i'll-be-fine-i've-got-more-important-things-to-get-on-with face. I waved you off and made myself comfy on the hard chairs (you know, the ones with the leather and the wooden arms and the straight back). Picking up the nearest reading material, I probably didn't even think about what was going on behind the closed door. I was too self-focused, too self-absorbed.

Hospitals always feel like you're on the cusp of being party to someone else's bad news.

You were in a room close to the entrance. I remember this because I remember vividly watching people come and go from the rotating doors. Wheelchairs were especially hard, it took a lot of manoeuvring of legs and wheels and feet to get in or out, to get through the threshold. There was a spiral staircase too - not a grand one - made out of metal and brown plastic bannisters. I never saw anyone use them. There was always a lift in motion though, ping, doors open, people out, people in, doors close, ping (but quieter heard from the other floors). Trying to understand it, taking myself away from the emotional baggage, looking to science for answers? The words are too hard and the papers too long. But a simple explainer surely can't encompass everything. The various treatments, vitamins, supplements, drugs, personal experiences and revelations, challenges in diagnosis and gender differences, the impact of toxic exposures, advancements in treatment, and the role of exercise, cannabis, and cognitive issues.

Mitophagy: the removal of damaged mitochondria via the PINK1 or Parkin pathway.

PINK1 is recruited to the membrane, and when it's healthy it removes pink1. if damaged, pink1 accumulates. This recruits parkin to the outer membrane,

adding ubiquitin chains to the membrane.

Once this accumulates enough it breaks down the mitochondria. 30-40 days of life for mitochondria. In PD, an abnormally high level of damaged mitochondria equals a decrease in healthy mitochondria. (but how?)

Mitochondria provide cells with energy, if they become damaged proteins on the outer membrane become tagged with these ubiquitin. So that it can be replaced. The pink1 accumulates on the outer membrane of damaged mitochondria.

Ubiquitin - controls the fate and activity of other proteins. It attaches to other proteins tagging them for outcomes within the cell. A linear sequence of 76 amino acids. They can form chains with each a different shape. They attach to proteins that need to be removed / destroyed / signalling immunity / signalling pink1 and parkin.

Genes that protect neurons in PD. ATF4 gene, switch to control mitochondrial metabolism (health).

Does it make sense to you?

It might make you small, it might make you
weak

But where there's a trough there's always
a peak

Put under pressure, changing without your
consent

A gem like a diamond you roll with intent
You're stronger than before, your strength
is infectious

Past, present, and future, you'll always
impress us

