THE CURE TRAP

Why the Most Funded Word in Medicine Keeps Failing Patients

By Benjamin Stecher

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A Note to the Reader

This book is for three kinds of reader.

If you live with Parkinson's, or love someone who does, this book is for you. It starts with my story because your experience is the measure of everything that follows.

If you are a scientist, in this field or any field where a good question got captured by a good word, this book is for you. The evidence is here, and the argument is meant to be taken seriously.

If you have ever given money to a cure (at a gala, in a will, in a moment of hope), this book is for you. You paid for this story. You deserve to know what it bought.

The book moves between memoir and investigation. At times it will feel personal; at times it will feel like an exposé. That is deliberate. The memoir is the spine; the investigation is what the spine carries. If a chapter feels dense, stay with it. The thread comes back to the patient, because the patient is the point.

Though this book is about Parkinson's, most of what it describes is not only about Parkinson's. The funding clock, the captured word, the broken ruler, the colony that answers to itself — that machinery runs across the whole landscape of neurodegenerative disease, and much of it applies to Alzheimer's with equal or greater force. I wrote about the disease I have. The arguments travel farther.

A note on how this book was made: I worked with an AI assistant through every stage of it — research, structure, fact-checking, and drafting. The ideas, the stories, and every judgment in it are mine.

One more thing, since this book proposes solutions: I do not claim to have one for every problem it names. Some are stated here, not solved, and that is not an evasion. As Anton Chekhov put it: "The task of a writer is not to solve the problem but to state the problem correctly." Where I could do both, I have tried. Where I could not, I have tried to do the second.

Introduction — Awake

Medical science is progressing slower than the rate at which the neurons in my brain are dying.
— Benjamin Stecher, *Being Patient*, 2020

They bolted a frame to my head with four screws.

Four screws, driven into the skull, two at the forehead and two at the back, to hold a metal cage perfectly still around my brain. I was awake for this. In my surgery, there was no sleeping through the part where they bolted the equipment to my head.

I sat in a chair and watched the nurse mark my forehead with a pen. An emergency case delayed me an hour, which I spent in the pre-op room trying not to meet the other patients' eyes. Then the operating room: the surgical team plus rows of students who'd come to watch, the table, the frame locked into its larger cage so my head couldn't move no matter what. Then half an hour of prep in a flurry all around me: the haircut, the sterilizing ointments, the oxygen, the mild sedative. Almost like a trip to the spa.



The Leksell frame locked in place, the author's view from the operating table, June 2021.

Then the drill. If any moment was going to induce trauma, it was that: the first time in my life I heard sound coming from inside my own head. It sounded like the entire world crashing together. One morbid plus is that I now know first-hand that there are no nerve endings in the brain. The drilling itself didn't hurt. Nothing past the scalp did.

This is how I got to deep brain stimulation: I let people drill holes in my skull and thread electrodes deep into the circuitry of my own mind, and I did it awake, because the surgeons needed me conscious to tell them what the electricity was doing to me.

To understand why I agreed to that, I have to show you what the mornings were like before.

By June 2021 I was taking about twenty pills a day. Each pill, if it absorbed properly, would flood my brain with dopamine and set off an hour of uncontrollable writhing, my limbs moving without my permission, like a marionette with a drunk puppeteer. Then, if I was lucky, about twenty minutes where I felt almost normal. Then the slowness and the tremor would creep back in, and I'd take

another pill, and the whole cycle would start again.

My neurologist, Dr. Alfonso Fasano, and I looked at that math together and decided it was unmanageable. Not him deciding for me. The two of us, patient and doctor, deciding together. That part matters, and I'll come back to it.

They threaded the electrodes into my brain. The frame came off, it doesn't stay on.

The programming didn't start for another month or so. Then Alfonso turned the current on for the first time, and I felt like the whole world had been lifted off my shoulders.

It worked. I want to say that up front, because this is not a book about a treatment that failed. Deep brain stimulation gave me my life back. I could button a shirt again. I could walk without thinking about walking, which is a luxury I didn't know I was living in until it was gone.

But here is the part that never makes it into the brochures: the switch being flipped was the beginning, not the end. What followed was tuning, iterative, painstaking, unglamorous work. Engineering, not miracle.

Alfonso and I wrote a whole book about that experience, *Reprogramming the Brain*. And the title was the point. Nobody cured anything. My Parkinson's was and is still there, still progressing. What happened over time is stranger and more interesting: my brain got reprogrammed. Tuned. Adjusted, month after month, by a patient and a doctor working as partners, until tomorrow started feeling better than today.

Hold that thought, because it is the entire thesis of the book you're reading.

I was twenty-nine when a neurologist told me I had Parkinson's disease. Old enough to understand exactly what it meant. Parkinson's doesn't kill you quickly. It just takes things, one at a time, for decades, and never gives them back.

What I didn't understand, what nobody told me at twenty-nine, staring at a brain scan, is that I had just enrolled, without consenting, in the most expensive vocabulary lesson in medicine.

The word was "cure."

In the years since my diagnosis, that word has raised billions of dollars. It has launched foundations, filled galas, named buildings. It has funded some of the most sophisticated science ever attempted on the human brain. And it has not cured Parkinson's disease. Not stopped it in anyone, not slowed it enough for any doctor to measure.

Let me be precise: I am not against curing anyone. The problem is the grammar. Oncology never cured "cancer." It cured cancers, one type, one subtype, one patient at a time. Real cures arrive in the plural, a small piece at a time. Parkinson's still promises the singular, and has delivered none of them: not one small cure for one biologically defined group of patients. That is the indictment.

This is the part where I'm supposed to tell you the scientists are corrupt or stupid. They're neither. I've spent ten years interviewing Parkinson's researchers and visiting labs around the world. They are, overwhelmingly, brilliant people working punishingly hard on genuinely difficult problems.

What's wrong is not the people. It's the trap.

"Cure" is the most funded word in medicine. So the money flows toward the horizon, toward elegant molecular theories, toward the beautiful idea, and away from the unglamorous work of making today better than yesterday for the ten+ million people living with the disease right now.

Now look at what actually changed my life. It wasn't a cure. It was two wires, a battery, and years of careful tuning: a technology born from tinkering, and from the monkeys whose brains showed us where to aim, refined through iteration, and aimed at a humble, measurable goal: make this patient's tomorrow better than his today. No gala was named after it. No billion-dollar campaign. Just engineering, attention, and a doctor who treated the patient as a partner instead of a subject.

That is the alternative this book is about. Not the capital-C Cure, but cures. Not the horizon, but tomorrow. Not the beautiful idea, but the tuned, tested, patient-verified reality of a life that works a little better than it did yesterday.

Underneath all of it sits a simpler belief, the one this book keeps returning to: lived experience should shape research priorities, and the barriers keeping patients out of the agenda are the problem to solve.

This book is my attempt to spring the trap. Or at least to describe it from the inside, because I have lived on every side of it: the patient who believed, the reporter who followed the money, the advocate who built a seat at the table, and the man with wires in his brain, trying to figure out who he is now.

Here's the map. Act I is the world as it was: the diagnosis, the word, the machine. Act II follows the money, five players, five seductions, and what I saw from inside each web. Act III is my education: a decade inside the science, and why the machine can't fix itself. Act IV is the intervention: the decision, the miracle, the price, the full story of the surgery this introduction only opens. Act V is the reckoning: what I built, and what should come next.

One warning, and one promise.

The warning: this book will make some people in my world uncomfortable. Good. Comfort never cured anything.

The promise: I'm not here to tell you to give up hope. I'm here to tell you where hope actually lives. It doesn't live in the word "cure." It lives in the smaller, harder, deeply unfashionable question this whole book is trying to answer: what would it take for every patient to feel a little better tomorrow than they do today?

Turn the page. Act I begins in Shanghai, with a twenty-nine-year-old who still believes the cures he hears.

Chapter 1 — Twenty-Nine

A year or so before my diagnosis, I'd already been a guest at Parkway Shanghai Hospital, one of those gleaming international hospitals for expats, floors that shine, doctors with perfect English, everything costing five times what it should. I went in with a double inguinal hernia and they assigned me a team of nurses on standby nearly around the clock for my entire stay. That's the level of attention money bought.

The first MRI happened at the same hospital. I lay in the machine, they took pictures of my brain, and then the doctor looked at my scan, looked at me, and told me nothing was wrong.

I believed her. Why wouldn't I? I was twenty-nine, building a company in Shanghai. Nothing was wrong. That's what the pictures said.

A few months later I was home on a trip when my mother, who had noticed my hand shaking, asked my aunt Rochelle, a GP, to come take a look at me. Rochelle booked me an appointment with a movement disorder specialist, Dr. Guttman, who diagnosed me almost immediately. He apologized before he said it, as if the diagnosis were a social faux pas.

Parkinson's disease. At twenty-nine.

Dr. Guttman advised me against going back to Shanghai. My symptoms were mild, a tremor here, some stiffness there. I thought, if this is Parkinson's, I can live with this. So being the stubborn, defiant kid I was, I went back. I had a great job there, and I was in love. She was pretty and sharp, and she didn't let me get away with anything. I thought we would grow old together. I wasn't going to let a word I barely understood rearrange my life.

We traveled together. I got to know her father; I introduced her to my mother. A year went by, and she stuck with me through all the shakes and bumps in the road. I thought she'd stick around for the rest of them too.

But it wasn't to be. We took a month apart to sort out what we each wanted. She, as any good millennial would, took to the internet, and found r/Parkinsons. She decided this disease would become too big a burden, and she didn't want to live with that kind of uncertainty. She wanted to be near her family and start a family of her own.

I wish I could say I handled it with grace. I didn't. I took my frustrations out on her in a series of nasty messages and emails until she blocked me completely. It was the darkest time of my life, made worse by my surroundings: expat communities are transient, and every month more of them were

leaving me behind. I wanted to die.

Here's the strange thing about the beginning: before any of that, the diagnosis itself hadn't bothered me much. It was abstract, the symptoms were background noise, and I carried on as though nothing had happened. Parkinson's doesn't announce itself. It just starts eroding things, so slowly you can almost pretend it isn't.

Almost.

The only people with Parkinson's I'd ever heard of were Muhammad Ali and Michael J. Fox. I remembered Ali lighting the Olympic torch in Atlanta, that quivering hand holding the flame. At the time it looked like defiance. Now, looking back at that video, what I saw was the future I was doomed to live: hands trembling, face frozen, barely able to walk, reliant on a fistful of pills just to make an appearance.

And then I started down the rabbit holes. When you're twenty-nine with an incurable brain disease and an internet connection, you will try anything. A traditional Chinese medicine practitioner taped poppy seeds to my ear. I don't remember what that was supposed to do. I remember believing it might help. He also told me to walk west for an hour a day. I never ran that experiment.

The list got longer over the years, bear bile, seal penis, glutathione, bird saliva, bee stings, ice-water immersion, high-dose thiamine, hypnosis, vagal nerve vibration, antifungal creams.

Early on I believed a lot of what I read, including some of the articles claiming a cure, not because I was gullible, but because the alternative is sitting still while your brain dies at its own pace. Desperation doesn't feel like desperation at the time. It feels like research.

It took two more years, but I eventually quit what had once been my dream job, running Ivy Track, the school I'd built from the ground up with a local coworker, and went home to seek an answer. The symptoms had progressed to the point where pretending stopped working. I needed to learn how to manage my health, and find out what therapies were actually on the way.

That's when the real education started. I read everything, every paper, every article, every word I could get my hands on. I was amazed by the pace of science, by the future it promised for humanity. I jotted down every word I didn't know; I built myself index cards, I turned neuroscience into a language, and my time in East Asia had taught me that I was pretty good at learning languages.

I also started noticing the same names repeated at the tops of the articles. So I started emailing them, telling my story, asking if they'd tell me theirs. I was amazed that some of them bothered to reply. Dr. Fasano did, back when I wasn't anybody to any of them. He took a keen interest, helped guide me

through the beginning, taught me the basics I needed to know.

I have since visited labs around the world and met many of the physicians and scientists working on this disease. But it started with index cards and cold emails, a twenty-nine-year-old kid who'd been told nothing was wrong, deciding to find out what was.

Chapter 2 — The Word

"Cure" is the most funded word in medicine. Not the most accurate, the most funded. It is specific enough to picture, distant enough to never arrive, and noble enough that questioning it sounds like cruelty. Who would argue against curing Parkinson's? Only someone who hasn't watched it take a person apart.

In 2018 I wrote a whole series called "The Search for a Cure." The field's direction could be summed up in two words: detect and stop. Detect the earliest signature of disease, stop it from advancing. That is the future most Parkinson's researchers are trying to build, and billions of dollars are being poured into making it real.

So what would that future look like for a patient walking into a clinic? The word "Parkinson's" might never even be used: it covers too broad a spectrum to be meaningful. You'd get a diagnosis that's a sub-subtype of a sub-subtype, a therapy tailored to your biology, and the whole ordeal reduced to a few doctor's visits. If broadly applied, it would pretty much eradicate the disease.

But that brave new world is likely centuries away. So what about the millions living with it today, and the millions more set to be diagnosed over the next twenty years? They get the word. The rest of us get the waiting.

The first steps toward it are more likely to look like what happened elsewhere. Cystic fibrosis is caused by variants in a single gene, yet its transformative medicines arrived class by class, matched to particular mutations. The first genuine cure for something filed under Parkinson's may likewise work in only a tiny, biologically defined subset. Alberto Espay, my co-author on *Brain Fables*, guesses the share could be as little as half of 1 percent. That would not make it a failure. It would make it a beginning, and proof that the umbrella diagnosis had concealed separate diseases all along.

Prove me wrong, researchers. Cure this disease.

However, here's the problem with the word: we may not even have the language needed to describe what we're trying to cure.

Each cell in the human body has tens of billions of moving parts, and we are made of thirty-seven trillion cells.

Humans look for order and meaning, and get drawn toward simple explanations over complex truths. So we confuse evidence for reason, and we reach for words that sound like understanding. "Disease-modifying." "Neuroprotective." "Cure."

Those words lack clear physiological definitions: you literally cannot put them on a drug label. But you can put them on a grant application. You can put them on a fundraising gala invitation. How do we claim to modify what we cannot define? Through subjective in-the-moment motor tests that output a single number. That's the entire edifice: a word with no definition, measured by a number we constructed, funded by billions.

And the machine that turns the word into money runs on headlines. A lab publishes a finding; out goes the press release; the headline announces a breakthrough. Companies get founded on headlines like that. Drug programs start because of them. The whole pipeline, two-point-six billion dollars per drug, twelve to fifteen years from discovery to market, set in motion by a slogan.

Meanwhile the metrics for success stay divorced from the human beings they're meant to serve. We measure H-indexes, a score researchers use to judge their contributions to science, instead of lives impacted. We fund promising papers that exist only to bolster journals.

All the while we forget what a patient actually feels. Not a mutation, not a pathway, only what they do to a body trying to get through the day. But there's no spring gala for "slightly less constipation."

So we continue to stumble blindly, leaving patients without a word to grasp.

Alberto Espay is a neurologist at the University of Cincinnati, my co-author on *Brain Fables*, and one of my closest collaborators in this field. He first described what I actually have as nigrostriatal degeneration, a much more accurate way to put it. That explains far more, and helps me understand why the prescribed treatments work. If this community described these diseases by the networks affected, we could match existing therapies to specific brain network dysfunctions far more accurately.

Honest words describe what's actually broken. Fundraising words describe what's fundable. As my uncle Felek put it: "Trying to cure Parkinson's is like trying to solve for world peace — both are pipedreams."

Chapter 3 — The Side Effect

I got invited to the Synuclein Conference in Lausanne, three days of the world's experts on alpha-synuclein, organized by Prof. Hilal Lashuel, who'd set the tone for open debate and unpublished data. Science as it should be.

Toward the end, I stood up and asked the room a question: what is our best evidence that these protein accumulations might be an effect of having Parkinson's rather than a cause?

There was some turning of heads, some muffled comments. Then one of the speakers noted that there are people with the disease carrying PINK1 and Parkin mutations who, upon autopsy, turned out not to have these protein clumps at all. With that, the room seemed satisfied, and the conference proceeded with the regularly scheduled programming.

But how could that be? The field had made it perfectly clear that these accumulations are the fundamental signature of Parkinson's disease. People with the disease but without the clumps should have been a crisis. Instead it was a footnote. The explanation came later, in a review I co-authored with Tilo Kunath: most people with PARKIN mutations never develop Lewy bodies at all. Their nigral neurons die on their own, by a mechanism that has nothing to do with alpha-synuclein. The contradiction was only a contradiction if you assumed Parkinson's was one disease. It isn't.

Moments like that piled up until I couldn't unsee the machine.

For most of my life I was a passive consumer of science. From the outside it looks like the ultimate storehouse of credibility, from which everything we know emerges fully formed. But I'd spent the last few years inside the house, browsing the section labeled "Neurology and Neuroscience — Subsection: Parkinsonisms." I'd read through many of its volumes, and even authored a few pages myself. And what I found was a narrative we'd created around misfolded proteins, driving almost every attempt to understand and treat the disease.

I don't say this to denigrate the work. The brain is hard. But science is a man-made system, and in it, evidence and theory mix to become beliefs that get hardwired into our cultures. The question is never just "what does the data say?" It's "what does the system reward?" Data never speaks for itself: it gets read through the story the researcher already believes. In Lausanne, the room heard data that should have been a crisis, and the story absorbed it as a footnote.

*

"That's it, that's the cure."

I stood squinting at the graph in front of me. Woah! The disease group really did fall back in line with the healthy controls. Maybe this target actually could swing the tides in our fight against Parkinson's diseases.

I watched the eager young researcher as he flipped excitedly through the rest of his slides. "Amazing," I said, not entirely certain I understood everything but wooed anyway by his enthusiasm and self-belief. "So, what's next?"

"Well, the journal wants me to run a couple more experiments in animal models and connect this to the field's belief in protein aggregation. Once it's published I'll be able to form a company through my university to develop bioassays to identify a lead compound. It shouldn't take more than five years to get it out of preclinical development."

At that moment, I knew I was screwed.

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The primary goal driving research today is not the progress of human knowledge or advancing society. It is publishing. To get published requires something novel, which does spur progress, but at a snail's pace, because progress has been rendered a side effect rather than the goal. Researchers are pressured into monopolizing data for a competitive edge, into telling clean stories with unambiguous results, into discarding the complexity that journals don't want. Scientists now spend an average of thirty-eight days writing a grant proposal. An estimated fifteen million hours a year go into reviewing papers that get rejected.

And the pipeline repeats the same flaw at every handoff: build something that works in a model, sell it or pass it on, let someone else run the next leg. Nobody owns the whole journey. Everybody owns their leg of it.

Those therapies have been built on stories we tell each other about what this disease is. Stories about misfolded proteins and aberrant pathways. Logical, compelling, fundable stories.

Which brings me to the sentence that should end every grant application but never does: doing more research is not the goal of research.

Patients today are still treated with the same drug their grandparents got in the 1960s. That's not the data's fault. The data has been screaming for years. It's the machine's fault, a machine that rewards the publication, the patent, the next round of funding, and calls the whole thing progress.

Progress is not the goal. Progress is the side effect.

Chapter 4 — The House That Cure Built

Nobody has done more to put a face on Parkinson's disease than Michael J. Fox. He took a diagnosis at twenty-nine, the same age I was, and turned it into the largest private Parkinson's funder on the planet, enduring everything the disease has thrown at him with a grace and humor that disarms everyone in the room. That counts. It counts enormously.

Which is why what follows isn't an attack on the man. It's an accounting of the house he built, and of the word written over its door.

The Michael J. Fox Foundation invented a playbook: venture philanthropy. Move fast, fund aggressively, demand milestones, treat research like a portfolio. It worked, in the sense that it mobilized billions and professionalized a field that had been sleepy. The foundation's defenders will point to PPMI, the Parkinson's Progression Markers Initiative, and they're right to. Fifteen years, more than $800 million by the foundation's own accounting, 50 sites, open data downloaded thousands of times a day. In 2023 it produced αSyn-SAA, the first validated assay for misfolded synuclein in spinal fluid. A genuine technical achievement.

The promise was cure. And the question the foundation has never had to answer is who decides what the money chases.

For twenty-five years, the answer has been the same small circle. Deborah Brooks co-founded the foundation with Fox in 2000 and was its first CEO until 2007. Katie Hood, who had joined in 2002, ran it from 2007 to 2011. Todd Sherer, head of research since 2006, risen from inside, was CEO from 2011 to 2021. Then Brooks came back. Four CEOs, twenty-five years, one circle. No outsider was ever given the chair. I'm not alleging corruption; I'm describing governance. A quarter century of billion-dollar decisions, made by people who have only ever worked for the house.

It can't just be Debbie and Todd in a room deciding where the money goes. It isn't. A lot of serious people run the science. The foundation employs some eighteen PhD scientists, led by chief science officer Mark Frasier and chief scientist Brian Fiske. It has an Executive Scientific Advisory Board carrying the biggest names in the field, Bloem, Marek, Kordower, Merchant, and two hundred and fifty outside advisors reviewed grants in a single year. Open calls, rolling industry review, milestone-based awards with go/no-go decisions. The machinery is impeccable. There's a Patient Council too, thirty-odd patients advising on strategy and education. They don't vote on the grants.

Here's the accounting, though. In 2026, the foundation renamed PPMI the Parkinson's Precision Medicine Initiative, same study, same acronym, new promise. The word over the door changed. The

study underneath it didn't. The promise got an upgrade; the study didn't. Fifteen years and more than $800 million later, what has a patient been told in a clinic that they weren't told before? Nothing. The assay is a research tool. It doesn't change anyone's care. That's not failure: it's measurement without translation, and it deserves to be named as such, because the money was raised on a different promise.

Which is what makes the record so damning. This isn't two people getting it wrong. It's the best-staffed, best-advised, best-funded Parkinson's operation on the planet converging for twenty-five years on the same theory, measuring the same markers, and producing nothing that changes a patient's tomorrow. The machine doesn't need two people in a room. It has hundreds. And it still can't tell me what my morning will feel like.

To be clear about what I'm not arguing: a patient with a vote on grants would not fix this. Put a patient in that room, same incentives, same theory, same endpoints, and the machine would produce the same grants. A seat at the table changes nothing if the table is still set for the same meal. What has to change is what counts as progress.

And the house kept funding the same story. The assumption underneath almost all of it, that understanding the molecular mechanisms of cell death will lead to cures, is, as Andrew Lees put it, "not justified on the basis of the last 50 years research." The synuclein hypothesis absorbed the lion's share. To be fair about the timeline: in 2010, that was a defensible bet. It was the best lead anyone had. My argument isn't that the first wager was foolish: it's that fifteen years later, with failed trial after failed trial behind it, the money was still flowing to the same table.

In 2023, I'd already said it in public. When the foundation announced αSyn-SAA with a celebrity video, Harrison Ford, Josh Gad, Jennifer Grey, the works, I posted the numbers they weren't leading with: 3.7% of healthy age-matched controls test positive; 12.3% of people with Parkinson's test negative. But the numbers were the smaller problem. The test answers yes or no. It cannot say how much disease a patient has, or whether it is getting worse, which is what a biomarker would have to do. Decades of synuclein research, and we still haven't established whether the aggregates drive the disease at all. "It is crucial that we are honest and clear in our communications and not give in to making exaggerated claims." The SAA could be a promising tool. It is not a biomarker for Parkinson's disease.

Which makes what happened in August 2025 worth sitting with: Alberto Espay, my own co-author, a man the foundation has funded, published a peer-reviewed refutation of the αSyn-SAA-based staging system, co-signed by Lees and others. His argument, in short: the markers are static, levodopa "reverses" the staging, the stages don't track any real measure of progression, and the whole construct is circular, "wherever the biomarker is found, the disease is assumed to exist." To MJFF's credit, they

funded the refutation too. That's honest science. It's also an epitaph for the flagship.

Which brings me to Michael himself, not the foundation, the man. Early on, he told Deborah Brooks: "The last thing I want is for you and I to find ourselves discussing our twentieth annual fundraiser. In fact, if that day ever comes you're fired." The foundation turned twenty on October 31st, 2020. The fundraisers continued. Nobody was fired. Somewhere along the way, the accountability got delegated, to the circle, to the process, to the next fundraiser.

We are the real experts on what this disease does to a life, Michael. Not the circle. Us, the ones awake at 3 a.m. because the tremor won't stop, the ones doing the math on how many good years are left. The billions were raised in our name. We'd like a say in what they're for, and in what counts as progress.

Chapter 5 — The Billionaire's Bet

In 2019, I helped the staff at Toronto Western Hospital put together a conference, the Revision vs. Reconstruction Symposium, and as part of it, we ran a writing challenge through my site, tmrwedition.com. The prompt: in 500 words or less, describe how you would spend a billion dollars for the sole purpose of accelerating knowledge about Parkinson's disease, or translating that knowledge into therapies that actually modify it.

Entries came in from everywhere. It was open to students and postdocs only, the people with the least power in the field and the freshest eyes. The winners got free registration and a trip to Toronto. I met people through that challenge who would shape my next decade of research, including Samuel Burke, then a student, now Dr. Burke, who would become one of my closest collaborators and stress-testers of ideas I have in the field.

It was a game. A hypothetical billion, and all of us just imagining.

Two years later, I was sitting in a backyard in Atherton, California, on what must be one of the most expensive pieces of residential real estate in America, across the table from the reason a real billion dollars was moving through Parkinson's research. I knew who I was going to meet.

A mutual friend had arranged it. Zenia arrived with her husband, Michael. She introduced herself as Zenia.

Zenia had been living with Parkinson's for more than two decades. It showed, in the way she moved, in the effort everything cost her. At some point I demonstrated my deep brain stimulator for her, switching the whole thing off and on so she could see the difference. She was impressed, but not overly impressed. I liked her immediately.

We talked for three hours. What I carried home wasn't anything she said about the disease. It was that she was still there, fully, sharply there, after twenty-plus years of it eating at her body. I was early in my own course and frightened of what was coming. She gave me hope that the person might survive the body.

Her full name was Eugenia Brin. Sergey Brin's mother, Sergey, the co-founder of Google.

What I didn't know was the chain of events she had set in motion. In 2004, Deborah Brooks heard that Sergey Brin's mother had Parkinson's. Through Andrew Grove, the Intel founder, himself living with the disease, an early advisor to the Michael J. Fox Foundation, she arranged a dinner: Grove and Sergey. Early the next year, the first large donation landed. In 2008, Sergey disclosed that he carries

the LRRK2 mutation, inherited from his mother. In 2019, the family's foundation launched Aligning Science Across Parkinson's, ASAP. Before ASAP, the family's money had flowed through the Fox Foundation, the first large donation, and years of giving after it. ASAP was the moment they built their own structure alongside it.

Sergey had said it plainly, years earlier, to Patrik Brundin: if he had to write a check for a billion dollars knowing it would lead to a cure, "it would be the easiest check I've ever written." The money was never the constraint. The question was always what it bought.

Follow the money backward and the river leads to one woman getting sick in 1998.

Here's what angered me then, and still does: at ASAP, the initiative her son's money built, almost nobody knew who she was. She was the backbone of what has become an entire field of science, funded by ASAP.

The science her son's money built had a human face. I knew Randy Schekman. I'd interviewed him in 2018, a Nobel laureate in cell biology, the founding editor of the journal eLife, and one of the sharpest critics of how science actually works: the top journals that won't publish challenges to their own papers, the impact factor he called a joke, the perverse incentives that send whole fields in the wrong direction. And he was chairing ASAP's scientific board for the most personal reason there is. His wife of forty-four years had died of Parkinson's.

Soon after Zenia and I met, I wrote to the friends who'd arranged it. I wanted to write an in memoriam, I told them she was the woman who had done more to catalyze Parkinson's research in the 21st century than any other human being, and I asked them to connect me with Michael and Sergey so I could interview them. They would have final approval over every word.

The reply came a few days later: they'd already asked Misha (Michael) and Sergey. They didn't want to do anything now. "It may change. I'll let you know when the time is right."

Eugenia Brin died on December 3, 2024. I don't know if the time will ever be right.

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In December 2022, after Forbes reported that Sergey had quietly given away more than a billion dollars to Parkinson's causes, I co-signed a letter with four others, Alberto Espay, Brian Pepin, Andrea Sturchio, Kariem Ezzat. Espay was my co-author; Pepin founded Rune Labs, where I chaired the patient board; Sturchio and Ezzat were Karolinska researchers and allies. "How Your Next $1 Billion can (Actually) Help End Parkinson's." We sent it through the same friends who'd arranged the Atherton meeting.

He never responded.

The letter, in full:

Letter to Sergey Brin – How Your Next $1 Billion can (Actually) Help End Parkinson's

Dear Mr. Brin,

Thank you for your generous support of the Parkinson's research community over the last decade. You've helped attract and train a generation of scientists to work on understanding Parkinson's, raised awareness of the disease, inspired hundreds of thousands of patients with hope.

However, despite these positives we do not have "a path to a cure", and more people than ever are suffering with Parkinson's. We want you to invest in a future where Parkinson's is treatable (or preventable), but think that there is a better way to spend your next $1 billion by focusing on three guiding principles:

Data from Parkinson's Patients is Key: We know Parkinson's is unique to humans, and that it can manifest differently even in patients with the same genetic mutation. The relevant data for learning how to end Parkinson's will come from Parkinson's patients directly, and we will need a lot of it. Startup companies are working to structure data across routine care and clinical trials (similar to precision medicine companies in oncology last decade) but there is need to support data-rich long-term registries that are essential for studying disease progression.

Evidence from Humans (not mice) Guides Mechanism Research: The track record of taking mechanistic discoveries in Parkinson's mouse models to humans is abysmal. Going forward, the discovery process should start from what we see in Parkinson's patients. One example of this human-first discovery approach is the "rescue" opportunity in restoring the low levels of proteins in the brain, as proposed in JAMA Neurology and visualized in this TEDx talk.

[In the original letter, "JAMA Neurology" linked to Espay and Okun, "Abandoning the Proteinopathy Paradigm in Parkinson Disease," JAMA Neurology 80, no. 2 (2023): 123–124, and "this TEDx talk" to Espay's TEDxWrigleyville talk, "Parkinson's and Alzheimer's: The Solution in Sight" (2022).]

More Parkinson's Care is a Win-Win. Most of what we have learned about Parkinson's has come from the trenches of clinical care, and we expect that to remain the case going forward. Unfortunately, there is a shortage of critical clinical resources for Parkinson's, including nurses, physical therapists, speech pathologists and neurologists. Helping to train and grow the next generation of clinical specialists to treat Parkinson's is a true win-win: improving our understanding

of disease and getting better outcomes for patients. New models leveraging virtual care can make this scale up capital efficient.

We ask that you please consider supporting the causes outlined above.

Sincerely,

Benjamin Stecher — Author, founder of Tomorrow Edition and chair of the Rune Labs' Patient Advisory Board

Dr. Alberto Espay — Professor of Neurology at the University of Cincinnati

Brian Pepin — CEO and Founder of Rune Labs

Dr. Andrea Sturchio — PhD student at Karolinska University and Research Instructor from the University of Cincinnati

Dr. Kariem Ezzat — Research Scientist at Karolinska University

Let me be precise about the money, because precision is the point. The Brin family office is called Bayshore Global Management, estimated on the order of a hundred billion dollars, run by George Pavlov since 2015. Pavlov was one of the few people at ASAP who actually knew who Zenia was. ASAP itself isn't a separate charity; it funds and administers its programs through the Michael J. Fox Foundation, the house from the last chapter and the Brin money are one pipeline. First grants: $161 million to twenty-one teams in 2020. Another $261 million announced in April 2026. Cumulative Brin-family giving to Parkinson's: more than $1.3 billion, making Sergey the largest individual donor to Parkinson's research, ASAP and MJFF together moving more than $350 million a year, more than the National Institutes of Health. This past April, Bayshore absorbed a brain-focused venture fund, Nexus NeuroTech Ventures. The bet is still growing.

I was in the room when they began figuring out where to aim it. In 2018, a year before ASAP was publicly announced, the Brin family foundation brought over fifty of the world's leading neuroscientists to Southern California for three days, plus a handful of patients, me included, to help decide what the money should chase. Four working groups, three days of argument about the biggest gaps in our knowledge of the disease. What struck me, sitting there with the disease going on in my own brain, was how much of it came down to belief. Smart, honest belief, but belief. That mapping the molecular causes of cell death would lead to cures. That synuclein was the driver. That what worked in mice would work in us. Leaps of faith, and then billions of dollars and countless hours spent following those beliefs.

And the bleak part, which I wrote at the time: almost nothing proposed in that room would reach a clinic within a decade. Turns out, I was overly optimistic. Nearly a decade later, nothing from ASAP has reached a trial, and nothing a patient could point to. There is an irony to the ASAP name.

Decades of work and astronomical sums had already gone into the basic science, and not one person had been cured: we didn't have a single thing that could even slow the disease down. I asked the question I've been asking ever since: can basic science solve a problem like Parkinson's on a timescale relevant to anyone living with it?

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Here's the thing the field won't say out loud: a funding stream bigger than the NIH's exists because one woman got sick and her son happened to be one of the richest men on earth. Not because the system worked. Not because peer review converged on the truth. Because a mother got Parkinson's.

And where did all of it go? At the same theory as everyone else's money. The machine I described in the last chapter doesn't run on the Michael J. Fox Foundation's dollars alone. It runs on hers too, $1.3 billion aimed at the same targets, measured by the same markers, producing the same nothing patients can feel. You could double or triple the investment in the same belief and nothing would emerge from it. Money doesn't turn incorrect ideas into cures. It is just more money going down the same drain.

That was the foundation money. The next thing I learned was how the institutions use their own money to court the patient voices that carry their message, starting with an invitation to Basel.

Chapter 6 — The Courtship

In October 2018, I spent two days inside the headquarters of the world's second-largest pharmaceutical company, and I came home and wrote it up like a dispatch from the inside. I published it on my site as "Notes From a Behind the Scenes Look at Roche." I want to show it to you, not the whole thing, just the load-bearing parts, because you need to see how the courtship works. I'll annotate as we go. Here is where they had me.

It started the way it always starts: with access. "I was given the chance to deliver a few talks and spend a couple days with people in the neuroscience division at the headquarters of the 2nd largest pharmaceutical company in the world, F. Hoffmann-La Roche Ltd, known to most simply as Roche."

That's the transaction, stated plainly: they gave me proximity, I gave them a patient voice to carry their message. Every player in Act II makes the same trade. Access feels like power, like you're in the room where it happens. It isn't. It's the appearance of power, extended deliberately, and it works because the alternative is shouting from the parking lot.

Then I did their PR for them, for free, on my own site. I gave them a loving corporate history: Fritz Hoffmann on the banks of the Rhine, "the birth of standardized medicine," a company that "has helped billions live longer, healthier lives." I was their unpaid communications department and I didn't even invoice them.

Then the humanization: "peel back the facade and what these companies really are is people, women and men working long hours to deliver the one thing that both the company and patients need to survive – effective therapies."

Every institution in this book is "just people." That will be said about the Fox Foundation, about the Brin operation, about all of them. And the book's answer is: yes. That's precisely the problem: decent people, incentives pointing elsewhere, and goodness doing the camouflage.

The companies I've visited have the best intentions, but they're constrained by market forces and investor interests.

Then I transmitted the gospel, in their voice, barely paraphrased: "They have chosen as their principal drug target alpha-synuclein, the protein whose aggregation is believed to be a cause of this disease." Their antibody, I reported, "should be able to slow disease progression and, in some people, potentially stop PD in its tracks." I added a perfunctory "many questions remain" and moved on.

That's how dogma travels: not through data, but through trusted intermediaries. I was a vector.

And then, this is the part that hurts to reread, the truth, in my own voice, buried mid-piece where nobody would trip over it: "There is a harsh truth that the PD world has to face – no one is working on a cure." And: "what about the seven million already diagnosed and hoping for a cure?"

I knew. Even then, I knew.

The piece's crescendo was patient power, my creed, which Roche let me chant on their premises while they made every decision without me: "We are the perfect counterweight to everyone else's vested interests." I closed by thanking Dr. Markus Britschgi by name, urging other institutions to "follow in Roche's footsteps," and signing off with the slogan: "No decisions about us without us."

I mistook being heard for having power. The courtship is complete when the courted start recruiting, and I was recruiting.

I still have the agenda Markus sent me for those two days in October 2018. Coffee and a campus tour. His lab. Lunch with three scientists from early R&D. Then two workshops, one with the prasinezumab project team, the antibody crew, one with the neurodegeneration discovery scientists, each built around a fifteen-minute talk by me, followed by Q&A. And the last item on the program: a meeting with their communications team, to quote the agenda, "to agree on how to work together on establishing the communication about Ben's visit at Roche."

The PR wasn't an afterthought. It was on the agenda. I was scheduled to be publicized.

Fifteen months later, they invited me back.

January 2020. Roche headquarters, Basel, Switzerland. This time I spoke to a packed auditorium of higher-ups, giving the talk I'd spent years assembling from all my others. Then they took me for a fancy dinner.

Here's what the machine did in return. It had me sign the paperwork, in which I was not a consultant or a collaborator but, throughout, "Patient." The paperwork said the point of the engagement was building relationships, and that I would share information about my new role in the neurology department at the University of Cincinnati, where I'd just moved to build a biomarker cohort program with Alberto Espay. I was paid a consulting fee, because I demanded to be paid beforehand. Too often, patients don't demand it.

And I handed them everything. The whole plan Alberto and I had built, the cohort, the biomarkers, the data strategy, all of it, in the hope that Roche might become part of it. I gave them a second plan, too: a fully drafted proposal to bridge the Western and Chinese Parkinson's worlds, a ten-week speaking tour and a research report on the state of the disease in China, the largest and fastest-growing PD population on earth. I was offering them China, the China Brain Project, my six years living there, my Mandarin, my three hundred contacts, gift-wrapped.

On February 16th I put it all in writing to their patient partnership director, the biomarker program, the China strategy, my network, and named my price for a consulting engagement. We'd agreed at Basel on a call between the Roche and Cincinnati teams in early March. Some preliminary discussions happened. Nothing materialized. The China plan is still unsponsored, six years later.

Here's what I've come to believe about what happened, not just at Roche, but everywhere in this book.

Biologists are plagued by their own tools. They can only see as far as their microscopes allow.

Think about what the field's instruments actually show. An electron microscope shows you protein aggregates in exquisite detail. It does not zoom out to show a person losing their ability to button a shirt. The tools resolve molecules, so the hypotheses become molecular. The synuclein bet keeps getting placed because synuclein is what the tools can see.

I said this once in a talk at McGill: the final frontier isn't outer space, it's inner space: we know more about distant stars than about what's happening beneath our skin. And the only models of Parkinson's disease we have are the people living with this disease.

Roche invited me to Basel to support the search for new biomarkers, new ways of seeing. I was, for two days, the best instrument in the building: a patient who spoke their language, who'd just built a cohort program, offering them China. Then they filed me under "Patient," took the plans, and went back to their microscopes.

To this day, their microscopes still show them synuclein.

There's a man who threads through this whole story, and his arc is the chapter in miniature.

Patrik Brundin invited me into the room where it happened: he brought me to the inaugural ASAP

meeting. I had first met him in his office at the Van Andel Institute, talking through what would become "Triggers, Facilitators and Aggravators," a paper Michaela Johnson and I co-first-authored, whose entire argument was that we have spent decades studying Parkinson's as though it were a single disease with a single cause. It isn't, we wrote. It's an umbrella term. He was a giant in the field, and he made room for a patient: he took my contributions seriously through every draft, fought for me to be first author when the journal noted it as improper, and later fought for my seat at the ASAP table.

In 2022, Patrik joined Roche as the therapeutic area leader for movement disorders, the division running the synuclein program. He also held a seat on the Fox Foundation's scientific advisory board.

I'm not imputing anything to Patrik. The facts don't need motives attached. The man who co-wrote "it's not one disease" now runs the one-target program at the world's second-largest pharma company by total revenue. That's not a contradiction to be explained. That's the machine, producing exactly what it rewards.

The receipts, briefly.

PASADENA was the first big test of prasinezumab, Roche's antibody against alpha-synuclein, the one I transmitted such hope about in 2018. It missed its primary endpoint: after fifty-two weeks, patients on the drug had declined no slower on the standard rating scale than patients on placebo. PADOVA, the larger follow-up, missed its primary endpoint in December 2024: it did not significantly delay confirmed worsening of motor symptoms. Roche pointed instead to a pre-specified subgroup, the patients already on levodopa, where the effect looked stronger. That subgroup is now the whole basis for PARAISO, the Phase 3: some nine hundred participants, all on levodopa, for a minimum of a hundred and four weeks.

Watch what happens after each failure. The population gets enriched. The trial design gets refined. The biomarkers get better. Everything gets interrogated except the hypothesis.

"No decisions about us without us." I chanted it in their auditorium in 2018. In 2020 I got my seat at the table, the invitation, the dinner, the applause, the paperwork with my name on it. And the decisions were still made without me. Or rather, the decision was made the way it's always made: the tools see what the tools see, the money follows the tools, and the patient in the room gets filed under "Patient" and thanked for his time.

The courtship worked. It just didn't work on the disease.

Chapter 7 — The High Priest of Synuclein

In the summer of 2018, I sent a cold email to a stranger.

His name was Hilal Lashuel, a biochemical neuroscientist at EPFL in Lausanne, and I wanted to interview him for my website about the intersection of chemistry and neurodegeneration. At the end of the email I added a second ask, almost as an afterthought: I noticed he was organizing a synuclein conference: would there be any patient representation?

He wrote back warmly. He'd be happy to be interviewed. And yes, they'd love to have Parkinson's patients at the meeting.

I wrote back the same day with ideas: the patient-engagement model I'd seen work at the ASAP meeting, a panel I wanted to propose called "Making the Connection: From Synuclein to Symptoms." He replied within hours: "There are great ideas."

A few weeks later he wrote: "I hope that this will be the beginning of lasting collaboration towards making research in neurological diseases more collaborative and patient-centered."

I held onto that sentence. You'll see why.

He was as good as his word, at first. He was genuinely excited to have us at Lausanne. I brought two other patients, Jon Stamford and David Ashford Jones, and all three of us felt the same thing: this man actually wanted us in the room. It gave me my first real jolt of inspiration, maybe bringing patients to the table could change the field for the better. The three of us took the stage, addressing his room, with the line "If you meet one person with Parkinson's disease, you've met one person with Parkinson's disease" projected on the screen behind us. He gave us the platform. The room listened. Later he took the whole conference out on a boat on Lac Léman, the sun setting behind Mont Blanc, during which we snapped a photo of the four of us with our arms around each other's shoulders, grinning like old friends.

The conference itself was remarkable. Lashuel put the field's ignorance on the agenda in plain language: What is the normal function of synuclein? How does the misfolding begin? Is the clumping part of the cell's defense mechanism? Are we certain it is even the cause of the disease? These weren't hecklers' questions. They were the program.

And I should say this plainly: the 2018 Hilal Lashuel was the real thing. That same summer he flew

to Colombia and spent a week with families living with Huntington's disease in difficult conditions, bringing medical supplies. He told me he'd been transformed by meeting patients: first at a Vatican event with 300 Huntington's families, where he looked around and couldn't find two patients with the same symptoms, then in Colombia. I believe he believed it, that involving us in research should become the bedrock of science, in his core.

The interview ran in two parts on my site that August. I want to walk you through it, because he said everything this book says, eight years ago, on the record, in his own words.

On heterogeneity: after the Vatican event, he asked "how can we as researchers trying to understand this disease be so focused on one molecule, or a few molecular mechanisms, in a disease that is so heterogeneous?"

On what matters: "We are so focused on finding a cure that we forget what the disease is all about... for the patients, the symptoms are the disease. That is what they deal with every day."

On incentives, and this is the one to hold onto: "the currency of researchers is secrecy." The system produces "science for scientists rather than science for society." Scientists "get trapped into this wheel." And his own litmus test, his words: "if I can't defend my actions in front of taxpayers and patients then something is wrong."

On the science itself: nobody can define a Lewy body beyond "rich in aggregated alpha-synuclein." The field uses "primitive tools to assess the pathology." And then the question that should have stopped the field in its tracks: "how can we succeed in developing cellular and animal models that reproduce the human pathology if we don't even fully understand what we are trying to model?"

On the central dogma, asked directly whether synuclein accumulation might be effect rather than cause: he was "not married to any specific hypothesis." Neurons, he conceded, can accumulate large aggregates "without any noticeable or measurable deleterious effects." There is, he said, "evidence for toxic, benign and protective effects."

And on the money: his synuclein protein library was "used extensively to advance several Michael J. Fox funded international collaborations," and "65% of my lab funding comes from patients-funded organizations. These people trust me with resources."

Read that list again. Heterogeneity. Symptoms are the disease. Secrecy is the currency. We don't understand what we're modeling. The aggregates might be effect, not cause. The money comes from patients.

He diagnosed the disease of the field. Then he went back to his lab, and the field carried on as before.

Men like Hilal defined what "leading science" looked like, and the funders holding the checkbook followed.

And then, in June 2026: his lab at Weill Cornell Medicine–Qatar was awarded $9 million over three years from ASAP, the Brin initiative, with Hilal as lead investigator, to "selectively target toxic protein aggregates associated with Parkinson's disease."

Nine million dollars to "selectively target toxic protein aggregates." Selectively. His own 2018 indictment was that the field lacks the tools to tell a toxic aggregate from a protective one in a living human brain, and hasn't even proven the aggregates are the cause rather than the fallout.

Nothing here turns on what Hilal intended. The record is enough. A scientist can believe every word he said in 2018 and still take the only check the machine will write him: nine million dollars to hunt the aggregate. The machine got exactly the science it pays for. He diagnosed it. Then the machine paid him to feed it. The tragedy isn't that he was wrong in 2018. It's that he was right.

Chapter 8 — The Colony

On June 4, 2018, I sent an email to Ekemini Riley, George Pavlov, and Randy Schekman. I had just come home from the first planning meeting for what would become Aligning Science Across Parkinson's, three days at the Balboa Bay Resort in Newport Beach, fifty-odd neuroscientists, a handful of patients, billions of dollars being aimed. I'd written up my notes from the meeting on my site, and the responses from both patients and researchers in the field had poured in. I thought the people running the initiative should hear what they were saying, so I passed their sentiments on.

The patients were frustrated. Frustrated by how long everything would take, by how little we seemed to know about the disease, by the exclusion of nutrition from the discussion. But they were also intrigued, by the idea of a roadmap, by the possibility of a genuinely collaborative effort. On balance, I wrote, patients were encouraged.

The researchers were a mixed bag. Many wanted to have been in the room. Some were skeptical about the initiative's true intentions. Many were optimistic it could move faster than I expected. A lot of them wanted details: what were the gaps, exactly, and what was the plan to fill them?

"Just wanted to share that with you," I wrote. "Hope you all have a productive start to the week."

Nobody replied.

One of the responses stayed with me. Lisa Vanderburg, commenting on my write-up of the workshop, put the patient's side of it in a sentence: "By the time the symptoms of a newbie PwP shows, no amount of our prior good 'health & lifestyle' amounts to a hill of beans in the face of this devastatingly complex disease."

I don't tell this story to embarrass anyone. I tell it because it's the cleanest picture I have of the thing this chapter is about. I did the job of a patient advocate: I gathered what the community was saying and carried it to the people with the power to act on it. And it went unanswered.

Here's what I've come to believe, eight years later: the problem was never any individual in that inbox. The problem is the structure they sit inside. Scientists have built an interconnected colony that feeds itself and holds itself accountable to itself alone. They are caught in a churn that too often produces science for scientists. Patient benefit is, structurally, a side effect.

I want to be clear because this isn't an accusation of corruption. I am not accusing any individual of doing anything wrong. In fact, they are to be admired for devoting so much of themselves over the last near-decade to a worthy cause. The problem is that the currency that progress is measured by

does not align with patient needs. Grants, publications, prestige, tenure, invitations, board seats. A career. The colony runs on career advancement, and it is very good at producing it, for its members.

Follow the connections. The Brin family's money, the $1.3 billion mentioned before, doesn't flow through a separate charity. ASAP funds and administers its programs through the Michael J. Fox Foundation, the one pipeline from Chapter 5. The initiative's Scientific Advisory Board, chaired by Randy Schekman, holds final authority over funding decisions. The same small set of names recurs across the planning councils, the steering committees, the grant programs. In the first grant wave, $14 million went to two teams at UC Berkeley, the SAB chair's home institution. (To be fair, and precision again matters here: the money went to other Berkeley labs, not Schekman's own. I checked.)

None of this is secret. It's all on public websites and in press releases. That's what makes it a colony: it doesn't hide. It just doesn't answer to anyone outside itself. The peer review committees that judge the grants don't publish their rosters. The final funding decisions rest with the initiative's own leadership and its own scientific board. The people who define what counts as leading science are, by and large, the people whose labs get funded to do it.

Dr. Kariem Ezzat, a close colleague and a neurochemist, put it to me this way after reading the early chapters of this book: the thought leaders define what "leading science" is, and the checkbook follows. People like Michael follow what the field's most prominent voices tell them is the frontier. The deeper problem, in Kariem's telling, is a culture among those voices that rewards show over substance, less creativity, less courage, more rhetoric. The observable part is what matters: the same theory gets funded, year after year, by the same interlocking set of institutions, regardless of what it produces for patients.

And this is where I have to steelman the other side, because the strongest objection to this chapter is also the most honest one. Dario Alessi, one of the sharpest biologists I know, told me in an interview that we understand less than one ten-thousandth of what there is to understand in biology. "We know virtually nothing about how biology is controlled and how it works." Funding bodies want shortcuts to drugs, he said, but "we don't have the fundamental basis that is needed to really solve these problems."

He's right. And here's the uncomfortable part: his argument is ASAP's founding charter. The whole initiative exists because Brin and Schekman and the planners in that 2018 room believed what Alessi believes: that we lack the fundamental understanding, and that only massive, coordinated basic science can build it.

So let me sharpen the question. It isn't whether fundamental science is necessary. I believe in basic

science: adaptive deep brain stimulation gave me my life back: that's a story for later in this book. My quarrel was never with science. It's with who science answers to. The question is whether a self-funding, self-reviewing colony can properly direct *which* fundamental science gets done, and to whom it answers when it doesn't work. Alessi says we need the fundamental basis. Fine. Who decides what counts as the fundamental basis? Who gets to say "this failed, try something else"? In the current structure, the answer to both questions is: the colony itself.

I want to name the exceptions, because they're load-bearing.

George Pavlov runs the Brin family office. He is, in a very real sense, the money. And he has always been responsive to me: every inquiry I've made, answered; generous with his time, including an in-person meeting at Bayshore's Palo Alto office and real engagement with my work, from the CCBP study to my investment inquiries. I proposed a Patient Advisory Board for Bayshore itself in May 2024. He declined: their existing outreach was sufficient, in his judgment. I disagree with the call, but it's his decision to make, not mine.

Ekemini Riley and Randy Schekman built ASAP: she ran the planning at the Milken Institute and was its founding managing director; he chaired the planning committee and has chaired its scientific board since. She now runs the Coalition for Aligning Science. They are the two most important architects of the machine I'm describing. I watched her walk into the planning room on day one, take the front of the room, and earn it within the hour: fifty-odd of the biggest scientists and egos in Parkinson's, and she ran them all. She let the heated arguments go where they needed to go without letting them turn vicious. In December 2021, Ekemini sat with me over coffee in DC and gave me what felt like all the time in the world, attentive, unhurried, genuine. In June 2026, eight years into knowing each other, she wrote to me about our shared journey and what my patient perspective had meant to the work. You can't fake that. If the colony were staffed entirely by careerists, she wouldn't exist.

Riley can respect the patient perspective all she wants, and I believe she does, but the structure she built still sent my 2018 email into the void. Pavlov can take every meeting I ask for, and I'm grateful, but the family office he runs still declined a patient advisory board. Good people, closed loop. To be clear, an answered email wouldn't have opened it. Neither would an accepted PAB.

An honest objection, because it's the first thing anyone inside the machine will say: patients do have a voice. They're invited to speak at every meeting. MJFF has its councils; ASAP brings patients into the room. All true. But there's a difference between being asked to tell your story and being given a vote. A patient slot on the program is not a seat on the board that decides where the money goes, and the councils patients do sit on too often end up as rubber stamps for decisions already made. Presence isn't power. The point is whether the patient perspective carries any institutional weight at all, or

whether it's decoration on a structure that answers to itself.

So here's the question the rest of this book keeps circling: a funding stream bigger than the NIH's, built by one family's money, governed by scientists who fund each other's science and review each other's grants, to whom is it accountable? Not to patients; we were in the room in 2018 and our email went unanswered. Not to the public; the deliberations aren't public. To the donors? The donors are patients' families and the public, and they were told the money would cure the disease.

There is one member of the colony this chapter has not named, and it is the one that makes the clock unbreakable: the regulators. The FDA and the EMA do not fund the two-to-five-year demand; they enforce it. A drug is approved on what it can show inside a trial with a fixed, short endpoint, so every trial is designed to read out on the clock, not on the disease. And the endpoints that count — a two-to-three-point change on the UPDRS, a marker moving in the right direction — are countable, which is not the same as meaningful. The regulators don't make the loop. They make it mandatory.

There is one more member of the colony, and it manages what the loop is allowed to say. The same interlocking set of names that judges the grants also referees the journals, programs the conferences, and awards the chairs. A dissenting idea doesn't just go unfunded. It goes unpublished, uninvited, unheard. As my neuropsychiatrist Mateusz Zurowski put it after reading this book, the system is frozen not only because the funders have a view of the illness and control the purse strings, but because they manage the whole loop of scientific discovery and discourse. Thomas Kuhn, the philosopher who gave us the term “paradigm shift,” named the mechanism more than sixty years ago: science is built to advance gradually, and it mistrusts the new. The paradigm shift is the exception. The colony doesn't need to conspire against new ideas. It just needs to keep doing what it was built to do.

The colony feeds itself. Nobody designed it to. It just never paid to do anything else.

Chapter 9 — Selling the Cure!

give it to us, not to rats or to fish

— Tom Isaacs, WPC 2016 closing song.

There's an objection to everything in this book, and I want to address it, because it comes from the people I respect most.

The objection is this: the ones selling "cure" aren't just suits in Basel boardrooms. They're people like me. Patients.

Tom Isaacs was diagnosed with Parkinson's in his mid-twenties. He walked 4,500 miles around the entire coastline of Britain to raise money and awareness, wrote a book about it called *Shake Well Before Use*, and founded an organization with the word right there in the name: The Cure Parkinson's Trust. He died suddenly in 2017, at forty-nine.

Likewise Michael J. Fox built the largest private Parkinson's funder on the planet on the urgency of a cure. I don't think I need to restate all that he has done for patients like me.

So here's the uncomfortable question, and I mean it sincerely: maybe they understood something about human nature that I haven't. Maybe you *need* to sell big hope, even hope you can't quite defend, if you want to achieve anything big. Maybe "cure" is the price of admission for mobilization.

I have sat with this for a long time. Here's my answer.

First, give the mobilization argument its due. "Cure" coordinates. It gives ten thousand people, scientists, donors, regulators, patients, one legible goal instead of ten thousand diffuse ones. It puts a poster on the wall. Nobody ever filled a ballroom by promising incremental improvements in activities of daily living. The billions exist because of that word. I'm not going to pretend otherwise.

Second, give the gentler version its due, the one thoughtful patients make. Why not both? Hope for the cure, raise money for the cure, and meanwhile do everything possible to live well today, exercise, community, the Davis Phinney playbook. The two don't have to compete.

They don't. My quarrel was never with hoping, and it was never with funding basic science, the device in my brain exists because basic science was funded, patiently, for decades. My quarrel is with the terms the hope is sold on. "Both" stays honest only while the cure half is: real timelines, real odds, the money accounted for. Sold the way it is actually sold, the promise doesn't sit peacefully beside living well today. It crowds it out. A better life permanently five years away is a reason to put

this one on hold.

But now the rebuttal, and it comes in four parts.

One: the moonshot fails when you don't know the physics.

The analogy everyone reaches for is Kennedy: he promised the moon, and the audacity of the promise is what got us there. Fair enough, except Kennedy's physicists knew the physics. Orbital mechanics was solved. The moonshot was an engineering problem dressed as a dream.

A Parkinson's cure is a dream dressed as an engineering problem. We don't know the physics. Hilal Lashuel, the alpha-synuclein field's own champion, admitted to me in 2018 that nobody can even define Lewy bodies, the field's central pathology, and asked how we can build models of a pathology we don't understand. Selling a moonshot without the physics isn't ambition. It's misdirection. It mobilizes resources toward the *performance* of ambition, the galas, the press releases, the pipeline slides, while the biology stays exactly as mysterious as it was.

Two: run the empirical test.

Here's the thing about "you need false hope to achieve big things": it's a testable claim. And it has been tested. The mobilization happened. The billions were raised. The armies were assembled, the galas were filled, the foundations were built, the word was said a million times. At the 2019 World Parkinson Congress in Kyoto, a thousand dexterity-impaired attendees were handed only chopsticks for lunch, all week.

The achievement didn't happen.

Not slowed, not stopped: nothing that changes the progression of the disease. If the theory were true, decades and billions of dollars of sold hope would have purchased *something*. It purchased an industry. That's the result. The theory failed its own experiment, and at some point, continuing to run it stops being optimism and starts being something else.

They'll say: science is slow, big problems take time, we haven't been given enough of it yet. Fair enough, biology is hard, and some problems do take decades. But "more time" only helps if the trajectory is converging. Ours isn't: the same hypothesis, funded the same way, measured by the same ruler, failing at the same rate. And "more time" never comes with a failure condition, no amount of time after which the field would concede the approach is wrong. That's not a scientific claim; it's a postponement. The question isn't whether science needs time. It's whether this program, run this way, has earned more of it.

Three: there is Isaacs' hope, and then there is the machine's hope, and they are not the same

thing.

This is the part I want to get exactly right, because Tom Isaacs deserves better than to be a rhetorical device. He was the real thing, diagnosed young, walked the coastline of a country, built something from nothing, died at forty-nine with the fight still in him. His hope was authentic. It belonged to him. I honor it, and I don't write a word of this chapter against him. I never got to meet him. On May 31, I emailed him asking if I could meet him on my UK tour. Later that day, I learned he had died.

But here is what happened to his hope after him, and this is the trap. When a foundation institutionalizes one man's hope into a perpetual fundraising engine, the hope detaches from the patient and attaches to the institution's survival. The organization now *needs* the cure narrative the way a body needs blood. It can't update, can't hedge, can't say "actually, the biology is harder than we thought, and your money might do more good elsewhere," because the machine runs on the promise.

So the question was never whether hope mobilizes. Of course it does. The question is who pays when the hope is false. The foundation keeps its endowment. The gala becomes annual. The people who pay are the patients, in the one currency they can't replenish, which is time. Tom Isaacs paid it. Every patient who donated to "cure" and died waiting paid it. At the World Parkinson Congress in Kyoto in 2019, someone pointed out that few people with Parkinson's seem to make it to more than three of them, and the in memoriam video grows longer every time.

And notice what researchers stake in the same gamble. Grants, replenished by the same system. Prestige, which survives a failed hypothesis. Career time, which still yields papers and tenure and the next grant. The machine pays them whether the bet wins or loses. Patients stake the one currency that can't be replenished, time, function, life. Same bet, different stakes.

There's a quieter cost to the promise, and it lands on us. When the whole story is "we're going to cure you," the patient becomes a problem waiting to be solved, something wrong with us, for other people to fix. Your life goes on hold. You wait. And waiting is not living.

I have seen that cost up close. People who raised the money, ran the races, told their stories on stage. I have watched them lose the will to live once they understood that the science they had worked so hard to fund was not going to help them. Not the next generation. Them. There are names I could put in this paragraph, and I won't. The people who could have agreed to be in this book are gone, and their families never signed up for it. The names stay out. The pattern stays in, because the pattern is the point.

I don't have a specific morning when it broke. There was no gala or headline that sold me and then went sour. What I had instead was meeting Alberto Espay and learning about the CCBP, it was revelatory, and working with him on Brain Fables, the book we wrote together. So much so that I

packed up and moved to Cincinnati for nine months to work with him.

Four: the choice was never hope versus despair.

What I saw in Cincinnati was the alternative: that the opposite of "cure" isn't giving up. It is *honest* hope.

Nobody promised to cure diabetes. Nobody promised to cure HIV. The great mobilizations against those diseases promised something else: *we will make this livable in your lifetime.* And they delivered, not through moonshots, but through the unglamorous, iterative, deeply unfashionable work of making tomorrow better than today, year after year, until a death sentence became a condition.

False hope has no half-life, not for the fundraiser. The money still flows; they're raising more than ever on the same promise. What decays is the patient: the trust, the time, the willingness to believe the next one. Perpetual false hope doesn't exhaust the machine; it exhausts the people the machine claims to serve, and leaves cynicism where the energy was. And the machine never runs out of patients. Our numbers grow every year, so there are always new patients to sell the promise to. The individual patient is irreplaceable; our population is replenishing. The promise never has to deliver: there is always a new audience. Honest hope compounds. A foundation that delivers a better tomorrow, then another, then another, builds the one asset no gala can buy: credibility.

The patients are already asking for this honesty. At Kyoto in 2019, a patient advocacy session reached consensus: stop showing only the content faces of people coping well, and start showing something closer to cigarette-warning depictions of the long, slow, painful death. One advocate pushed back, it could stigmatize patients and terrify the newly diagnosed, but the demand in the room was for honesty over comfort.

What we can't handle, what I can't handle, is being sold the same hope forever, by people who know exactly what they're doing.

Tom Isaacs sang it at the World Parkinson Congress in 2016, and I'll leave the last word to him.

There's a breakthrough out there, but there's one thing I wish: that you gave it to us, not to rats or to fish.

Chapter 10 — Journey Round My Brain

Patients are the best teachers a doctor will ever have.

Chapter title is borrowed from Frigyes Karinthy's A Journey Round My Skull (1939), his account of a brain tumor and the surgery that removed it (skull for brain).

In the summer of 2016 I went to the World Parkinson Congress in Portland, Oregon, about five thousand people, patients and researchers and clinicians and caregivers in one place. I had been diagnosed two and a half years earlier.

I watched Tom Isaacs sing at the
closing ceremony, a patient, on stage, singing to the researchers about bridging the divide between them. What Portland gave me was a launching point and a determination to go see the science myself. Not wait for it to come to me. Go to the labs, meet the people, look down the microscopes, ask the questions a patient would ask. Over the next year I travelled to labs all around the world and wrote it up as a series called "Journey Round My Brain." This chapter covers the highlights of that journey: what I saw, what I learned.

I paid for that education myself. In my twenties, working in China, I had saved almost a quarter of a million dollars. I spent almost all of it traveling to labs to teach myself about this disease.

North America: the first lab.

The first lab I ever visited was Jeanne Loring's, in San Diego. Loring is a stem cell biologist at Scripps. I credit her and Andres Bratt-Leal with giving me my first guided tour of neuronal cell cultures and the miracle that is induced pluripotent stem cells (iPSCs): take a few skin cells from a person, reprogram them into stem cells, then direct those stem cells to become any cell type in the body. In Loring's lab, the target was dopamine-producing neurons, grown from a patient's own cells, to be transplanted back into the patient's brain to replace the cells Parkinson's had killed.

I had never seen anything like it. You have to understand where I was coming from. I had spent years reading about this disease in the abstract, genes, proteins, pathways, papers. In Loring's lab I was looking at the thing itself: cells, in a dish, being differentiated into the very thing I was losing. The work was funded and driven in part by patients themselves, through an initiative called Summit for Stem Cells, patients who had educated themselves through lab tours and decided to push the science forward rather than wait for it.

From San Diego the tour widened. In San Francisco, Steve Finkbeiner's lab at the Gladstone Institute was tackling a different problem: the models were wrong. Researchers were testing therapies on rodents and dishes that didn't behave like human disease, so Finkbeiner's team were using iPSCs plus machine learning, to autonomously photograph cells at every step, with algorithms finding patterns no human could see.

In New York, Lorenz Studer's lab at Rockefeller was the closest, by my reckoning, to a human stem-cell replacement trial among the labs working on it, and Studer himself embodied the cautious optimism the whole field needed: hopeful, exact, allergic to hype. The science he was working on would become BlueRock Therapeutics, whose embryonic-stem-cell-derived therapy is already enrolling in Phase 3.

And through online forums I met Sara Riggare, a patient and researcher, who gave me the number that has organized my thinking ever since: patients typically see a movement-disorder specialist for one hour a year, while living with Parkinson's for the other 8,765 hours. 1 vs. 8,765. Those numbers crystallized a thought: patients have no choice but to arm ourselves with the tools needed to actively engage in our own care.

I also saw, even then, the constraints. Researchers were working under budget cuts, strict grant timelines, mountains of paperwork, heavy patient loads, and still giving a patient who had cold-emailed them an hour of their time and a free education. Progress, I wrote, is human labor and ingenuity, and scientists need money and time and resources. That observation would take years to become the argument of this book.

Israel: the mannitol trap.

Israel was the fitting first international stop. I was born an Israeli citizen, and Ashkenazi Jews carry a higher risk of Parkinson's and a higher carriage of its associated mutations. The science there was excellent. But what Israel taught me was not science. It was economics.

In Tel Aviv I met Daniel Segal, who had found that mannitol, a common sugar alcohol, already approved as safe, already sold as a food supplement, could prevent alpha-synuclein clumps from forming. Patients were reporting symptomatic benefits. And yet mannitol was unlikely ever to reach the clinic. Physicians only prescribe trial-validated treatments, trials take years and tens of millions of dollars, and mannitol is already Generally Recognized As Safe, so no company can profit from funding a trial. Nobody owns it. Nobody will pay to prove it. The dose and the best stage for treatment may never be answered, not because the science is hard, but because the economics are

impossible.

I did not have a name for it then. I do now: the ownership trap. A system that only tests what it can sell will never test what it cannot own, however promising it looks. In Israel I also saw the workaround: citizen science, patients running their own trials, campaigns like CliniCrowd. When the evidence system fails patients, patients run their own personalized, self-funded trials. That is not a failure of patience. It is a failure of the system.

Mannitol is the drug that cannot be owned. But most drugs can be, and there is a bargain underneath those — one fair deal in the system, worth stating plainly. Peter Kolchinsky of the investment firm RA Capital calls it the biotech social contract: society grants a company a temporary monopoly, a patent, and in exchange, when the monopoly expires, the drug goes generic and becomes cheap forever. As my collaborator Sam Burke puts it, "we give those who make patents the right to a monopoly for a fixed set of time for them to then open source the technology." The deal works when drugs can go generic. Kolchinsky himself warns it breaks for the ones that can't — cell therapies, gene therapies, the complex biologics. That is where the future of Parkinson's treatment lives.

And the deal has a second break, on the other side of the counter: it assumes someone pays the monopoly price while it lasts. In America, someone mostly does. "The US has underwritten basic science and drug discovery for the whole world," Burke says — which is why every company wants American approval first. Everywhere else, the payers have learned to be stingy. Britain prices a year of life in advance and calls it a QALY. Canada's formularies do the quiet version of the same arithmetic. I am not saying the math is simple. I am saying the circle it makes is vicious: the fewer payers willing to pay, the fewer there are to split the fixed cost of inventing the drug, so the price must be higher, so the payers get stingier. "When people aren't willing to pay for treatments, well, then you have to charge more, because it still costs the same."

Canada gave me the anecdote. Alex Shved was thirty-seven, a father of two in Etobicoke with stage-four melanoma, and the treatment his physicians wanted for him was tumour-infiltrating lymphocyte therapy in Florida: US$515,000 for the treatment alone, the hospital stay extra. Ontario said no, three times, on the ground that the out-of-country program isn't bridge funding for drugs that might one day get public coverage. He took the province to court and won: the judges quashed the denials as unreasonable, noting on the record that he would likely be dead by Christmas without treatment within weeks. Health Canada had approved the therapy the previous August. It still isn't available here outside clinical trials.

The same therapy had arrived a different kind of too late a year earlier. Evan Armit was twenty-three, an elite hockey player from Dryden, Ontario, dying of metastatic melanoma. His doctors backed his

application to Ontario's out-of-country program for TIL therapy at the Dana-Farber Cancer Institute in Boston. OHIP said no, twice. His father wrote the Premier's office. Evan died on August 24, 2025, days after Health Canada approved the therapy that might have saved him. The final appeal was denied four days later.

In Jerusalem I visited Tikvah for Parkinson's (Hebrew for 'hope'), founded by Debbie Shapiro after her own diagnosis, when no site in the city offered a full package of Parkinson's therapies. Tai chi, speech therapy, physical therapy, exercise, art classes, and above all a peer community. It was one of the best patient centers I had ever seen, built by a patient, not a hospital. Years later, when I started arguing for intensive therapy centers as the model of care, Tikvah was part of my argument.

England: patients as participants.

I framed the England leg as a letter to James Parkinson, two hundred years after he described the shaking palsy. Little progress on the disease itself, I reported, but the country was buzzing, and what inspired me most was the determination of English patients: impatient with impersonal large organizations, unwilling to sit around waiting for doctors to fix things.

In London I visited the Royal Free's genetics team, twenty PhDs working on the genetic forms of Parkinson's, including the N370S GBA variant that I carry myself. They were running an Ambroxol trial, and the point was one I would carry into this book: researchers were no longer treating Parkinson's as one disease. They were targeting specific variations.

Another spotlight was the grassroots. There was Spotlight YOPD and the South London Younger Parkinson's Network, organizations built specifically for young-onset patients, whose needs differ from later-onset disease. The European Parkinson's Disease Association, linking patient groups across nearly thirty countries. Linked Clinical Trials, Richard Wyse's project at the Cure Parkinson's Trust, repurposing existing drugs and matching combinations to patient cohorts, a model for the personalized-medicine era, away from one-size-fits-all.

And there was Tom Isaacs. I never got to meet him. Chapter 9 tells that story. But what belongs here is his point: patients are not simply lab rats, but active participants in shaping research and clinical trials. In England I saw that point made real, patients building the organizations, the networks, the trials, themselves.

And there was Jon Stamford, first introduced in Chapter 7, a neurochemist who had spent his career studying dopamine, then was diagnosed with young-onset Parkinson's himself, and became a patient

advocate. He had lived both sides of the divide: the researcher who studies the disease, and the patient who lives it. Talking to him, I heard the argument of this book in embryo, that lived experience should shape research priorities, and that the barriers keeping patients out of the agenda are the problem to solve.

England also gave me the caution I needed. John Hardy, the geneticist, told me the story of cystic fibrosis: the gene was identified in 1989 and was expected to lead to a cure. It led to better care. Parkinson's now has forty-plus known genetic variants with still no approved therapy from any of them. And Roger Barker, the stem-cell researcher in Cambridge, embodied cautious optimism: the 1990s fetal-cell trials had mixed results, and new trials were justified only by better understanding of cell type, culturing, storage, implantation, and patient selection. Hope, yes. Hype, no.

Edinburgh: openness.

Edinburgh was the last leg of the published journey, and it gave me the contrast that organized everything I had seen. At the Anne Rowling Regenerative Neurology Clinic, Siddharthan Chandran had built a center that brought neurodegenerative diseases together under one roof, since they overlap in symptoms and causes. Chandran believed the answers lay in the patients themselves: patients as integral parts of research, active participants in trials, donating tissue, engaging researchers. Each diagnosed person, he said, holds part of the puzzle.

Tilo Kunath's lab was the same story in a different register: patient engagement plus global collaboration, growing dopamine cells from embryonic stem cells for safe transplantation. Ken Bowler ran a group that brought patients into research through dialogue and seminars. Everywhere I went in Edinburgh, the doors were open. I contrasted it, in my notes, with what I would go on to see in "closed-lip centers" in much of Europe and Asia: places where the science was guarded, the patients were kept out, and the collaboration stopped at the lab door.

Germany: the boat with multiple holes.

From Britain the journey carried on into mainland Europe, where I spent four months in southern Germany learning from Prof. Gerold Riempp. Gerold was a professor of information systems who was also living with Parkinson's, and he studied the biology of his own disease the way a systems architect maps a failing network. If the labs in San Diego, London, and Edinburgh had shown me individual pieces of the puzzle, those four months with Gerold were where I learned why no single piece was ever going to be enough.

Walking through the literature with Gerold day after day, Parkinson's stopped looking like a single domino falling and started looking like simultaneous systems failing. This disease is not just a

protein clumping disorder, or just a mitochondrial energy disorder, or just a lysosomal and autophagic waste clearing disorder, or just neuroinflammation triggered by a mix of genetic and environmental hits. By the time a person walks into a clinic with a tremor, it is almost always several of them at once, fueling one another inside the same brain.

Picture a degenerating brain as a boat with multiple holes in its hull, a different combination in every patient. One hole might be mitochondrial failure; another, impaired lysosomal autophagy; another, chronic neuroinflammation or synaptic decay; and still others, environmental or viral hits that weakened the timber years ago. Now watch how the pharmaceutical industry tests a "disease modifying" drug. A company develops a molecule designed to patch a single hole, say, clearing extracellular synuclein or boosting one lysosomal enzyme. They run an eighteen month monotherapy trial, rather than testing cocktails that plug multiple holes at once the way oncology and HIV learned to do decades ago. And when the boat keeps taking on water through all the other open holes in the hull and sinks at nearly the same rate, they declare the patch a failure and throw it away for good.

By December 2018, after I had left Germany, that realization had soured into anger. Watching companies recruit patients into one doomed monotherapy trial after another felt like watching people being asked to bail out a sinking ship with a teaspoon, and I was tempted to use my platform to call for an outright boycott. Before I said or wrote something so drastic that I might later regret it, I wrote to Gerold to ask for his guidance. Since we shared the view that clinical trials would only succeed if they adopted an adaptive, combinatorial design, should I start urging patients not to join monotherapy trials at all? Gerold counselled patience. He reminded me that the flaw wasn't a lack of goodwill among researchers, and that many patients join trials simply for the closer neurological care they receive inside them; our real task was to prove to the community that an adaptive combinatorial approach was by all means the better option, because in many cases Parkinsonian symptoms arise from an individual combination of cofactors, and a one size fits all therapy will likely only help a portion of patients, if any. "Well reasoned my friend," I wrote back. "Thank you for always providing sound guidance."

Eight years and dozens of failed monotherapy trials later, the evidence is in. Until we stop testing one patch at a time on a hull with multiple holes, single target drugs aimed at slowing progression will keep failing, no matter how solid the science behind that one target may be.

San Diego: a decade on.

The journey began in a lab in San Diego, watching cells being differentiated into dopamine neurons. A decade later, that promise has a shape and a price. The company that grew out of Loring's line of work, Aspen Neuroscience, filed to go public in October 2026, up to a hundred million dollars, Nasdaq, ticker ASPE. Its lead therapy, sasineprocel, is an autologous iPSC-derived dopamine neuron

replacement: your own skin cells, reprogrammed, grown into dopamine neuron precursors, implanted into the brain. In an open-label Phase 1/2a trial, fifteen patients dosed, the March readout showed improvements in symptom control, motor function, and quality of life at one year, and some patients were able to reduce their levodopa. Phase 3 dosing is expected in the second half of 2027.

That is real. It is also slow. In 2017 Loring targeted a trial start in 2019, and the cell-replacement field talked about therapies widely available in five to ten years. It is 2026, and we are at Phase 1/2a. The wonder was real. The timeline was not. That gap, between what the science promises and what the apparatus delivers, between the cells in the dish and the patient in the clinic, is the gap the rest of this book is about.

At the end of that grand tour, I emailed a question to the experts I'd met: if perfect knowledge of the brain is a hundred-yard race, where are we? The consensus was humbling. Right around the ten-yard mark. We know almost nothing, and we are very good at pretending otherwise.

What the journey taught me, in the end, was a pattern. Wherever the doors were open, Edinburgh, San Diego, the patient-built centers, the collaborating labs, the science was better, the patients were stronger, and the work moved. Wherever the doors were closed, the work stalled, and patients waited. I did not set out to learn that. I set out to learn about my disease. The journey taught me about the machine instead.

Chapter 11 — Counting the Lights

I didn't need a paper in the summer of 2026 to tell me what Sam Burke had been telling me for years. But the field did. It was a preprint meta-analysis from the Skene Lab at the UK Dementia Research Institute, not yet peer-reviewed, the most comprehensive study of its kind. The team had scoured sixty years of post-mortem evidence: 166 case-control studies, published between 1963 and 2025, comparing patients against healthy controls across 145 distinct region-cell populations, to see exactly where the biological wreckage occurs.

The headline finding was striking enough. The noradrenergic neurons of the locus coeruleus, the cells that regulate alertness, attention, stress responses, and sleep-wake cycles, degenerate at almost the same rate as the dopamine neurons of the substantia nigra. There was significant loss of cholinergic neurons in the forebrain, too, the cells tied to memory and cognition. The dopamine story, the one the field has told for sixty years, is partial.

But the deeper finding was the one that stopped me. Despite decades of research, we still don't actually know if the affected cells die. The vast majority of studies count markers, tyrosine hydroxylase, melanin, ChAT, rather than neurons themselves. A marker is a light in a window. A dead cell is a dark building. A cell that has simply turned off its identifying features is also dark. Counting markers cannot tell the two apart. We have been counting the lights in the windows of a city, not the buildings themselves.

I called Samuel Burke. Sam is a co-author on the paper, and he has played an outsized role in my thinking about this disease ever since we met through the 2019 writing challenge. For now, the point is that Sam is the person who taught me to ask the question this chapter is about: not what the evidence says, but whether the evidence was ever counted right in the first place.

The seed.

I had heard the counting problem before, years earlier, in a different register. In 2018 I interviewed Ted Dawson, who studies neuronal survival and cell death. Dawson's point was that the field cannot reliably distinguish a dead dopamine neuron from a merely dysfunctional one, a cell that is still there, still alive, but no longer doing its job or showing its markers. The distinction matters enormously. A dead cell can only be replaced. A dysfunctional cell might be revived. If your counting method cannot tell them apart, your entire picture of the disease, how fast it progresses, what kills, what might be saved, is built on sand.

Dawson added a second point, about why the sand never gets shoveled away. The grant system

forces short studies on short-lived animal models, quick, cheap, publishable, and short studies cannot answer long questions. Here, the point is narrower: the way we fund science shapes what we count, and what we count shapes what we believe.

What we didn't count.

The Skene paper was a reckoning with sixty years of counting. But the counting problem is older and wider than one meta-analysis. When I interviewed Beth Stevens, who studies microglia, she told me that activated microglia had been reported in the substantia nigra of Parkinson's patients for nearly a century, and the field had only recently started studying them. A century of evidence, ignored, because it didn't fit the dopamine story. Stevens put the model problem plainly: our models don't accurately reflect what is happening in humans.

Ricardo Dolmetsch, who ran neuroscience at Novartis, said the same thing from the industry side: "We learned a lot from them [animal models], but many things were not translatable to humans." The models are not useless. They are untranslatable in the ways that matter most, the ways that would tell us whether a treatment that works in a mouse will work in a person.

And then there is the data itself. The Skene team tried to stratify their findings, body-first versus brain-first progression, LRRK2 versus GBA versus cases with no known cause, disease duration and its effect on specific cell loss. Each attempt came up short. Not because the researchers weren't diligent, but because the clinical data is too sparse to support the weight of these questions. Only 4 of the 145 populations were adequately powered. Eighty-two percent of Allen Brain Atlas regions have never been quantified in Parkinson's disease at all. We are decades into the study of this disease, and the raw data left behind by previous generations is too thin to build a bridge to personalized medicine.

What measurement costs.

So far this chapter has been about researchers and their data. But measurement is not abstract. I know what it costs, because I have been on the other side of it.

I joined PPMI, the Parkinson's Progression Markers Initiative. Part of what PPMI measures requires lumbar punctures: a needle into the spinal canal, to draw the fluid that might carry the disease's fingerprints. I told this story in Brain Fables. My lumbar puncture took forty-five minutes. There was no follow-up. The pain in the region persisted for months afterwards. I dropped out.

That is too often the price of the data, paid by patients, in their bodies.

The ordinary measurement is less dramatic and more grinding. Twenty minutes every six months

with a neurologist, just enough time to go through an awkward series of motor tests. That is the clinical encounter, the unit of measurement on which the whole apparatus runs: twenty minutes, twice a year, to assess a disease you live with during all the hours in between. Michael J. Fox, at a talk in 2017, called the Unified Parkinson's Disease Rating Scale, the UPDRS, the field's standard, an "elaborate drunk test." He was not wrong. A scale that asks a patient to tap fingers and walk a line, scored by eye, is the instrument by which billion-dollar treatment decisions get made, and on it, higher is worse: the number climbs as the patient declines.

Riggare calls this "diabetes envy." People with diabetes have clear measures for their current state, blood glucose, and for their long-term progression, the HbA1c test. Parkinson's has nothing comparable. Riggare's deeper point is about incentives: "The key is to find ways to measure things that help people make meaningful choices about issues that are important to them. Currently, the frenzy is to market products that measure things that are easy to quantify, regardless of whether they help people or not." We measure what is countable. We call it progress.

The stakes.

Why does any of this matter beyond the laboratory? Because the counting crisis is not an academic embarrassment. It is the reason the medicine cabinet is empty.

Between 1999 and 2019, the field ran 357 Parkinson's trials testing 152 compounds. The failure rate was 85.1%. Read that again: for twenty years, nearly nine out of ten attempts failed. Some of those failures were bad drugs. But some of them were good drugs tested against bad measurements: treatments judged by scales too crude to detect their effects, in trials too short to see them, in patient populations too heterogeneous to respond as one. When your ruler is wrong, you cannot tell a failed drug from a failed measurement. And when you cannot tell them apart, you throw out both.

This is the cure trap in its most concrete form: a cure promised on a deadline, and the deadline now running the science. The apparatus demands answers in two to five years for a disease that takes decades to reveal itself. It counts what is countable, markers, motor scores, two-to-three-point changes on the UPDRS, and calls the result evidence. The evidence is then used to justify the next round of funding, the next round of trials, the next round of counting. The loop is closed. The patient is stuck outside.

The Skene authors did something else that should be standard: they simplified and translated their work into plain English, and they built an interactive website with a walkthrough for anyone who wants to understand it. Transparency is not a courtesy. It is the precondition for counting anything honestly. If every paper came with a plain-English translation and an open walkthrough, the counting crisis would be harder to hide, and easier to fix.

We have been counting the lights in the windows of a city, not the buildings.

Chapter 12 — The Umbrella

Parkinson's disease does not exist. No one has found it in a brain, recreated it in a dish, or given it to an animal. What we have are people living under a clinical label.

I wrote "seven million" once, in 2018, for the number of people already diagnosed and hoping for a cure. That number is dated now. The Global Burden of Disease study counts 11.77 million people living with Parkinson's in 2021, up from 3.15 million in 1990. The count keeps climbing. What hasn't kept up is the understanding. This chapter is about why: the umbrella shelters not one disease, but many, and trials designed for one disease cannot cure millions.

The umbrella term.

We proposed this in 2018, in a paper on triggers, facilitators, and aggravators that I co-authored with Michaela Johnson, Viviane Labrie, Lena Brundin, and Patrik Brundin: Parkinson's is an umbrella term, not one disease. The triggers that start it, the facilitators that let it spread, the aggravators that make it worse, these differ from person to person. If the pathology has already developed beyond the facilitator phase, just targeting the facilitator may have minimal effect. Treat the umbrella as one disease, and you will aim at the wrong target in most of the people under it.

A year before that paper, I asked ten sharp minds across the Parkinson's world, including Gerold Riempp, my teacher from those four months in southern Germany, for the most important unanswered questions in the field. Their answers told the story better than any argument I could make. Gerold asked: "Is PD really a single illness or is it rather a group of different ailments that all lead to somewhat similar symptoms in the end?" Prof. John Hardy asked whether alpha-synuclein deposits are the cause or consequence of something deeper wrong with neurons. Prof. Roger Barker asked when Parkinson's disease even begins. Nine years later, those questions are still open.

Tony Lang, no outsider; he runs the movement disorders program at Toronto Western, said the same thing on the record in 2018, without needing the umbrella metaphor: the field was not dealing with a single disease, but with multiple diseases. His forecast was incremental: a therapy that works in five percent of patients, then another five percent, no single home run.

I revisited the hypothesis in 2022. The revision kept the core, not one hit, many, but changed the sequence: triggers, then inflammation, then cell dysfunction, then the tipping point. It broadened the frame from Parkinson's to the neurodegenerative spectrum, and I dropped some of the 2018 categories that no longer made sense. The biggest shift was the target: not the cell, but the circuit. The question became how much circuit dysfunction it takes to reach the tipping point, and whether

you can protect, slow, or restore the circuit's function. The disease develops over a long prodrome, likely ten to twenty years before symptoms. By the time anyone notices, the hits have been accumulating for decades.

In *Brain Fables,* Alberto and I wrote that we hoped it was one disease and feared it was a spectrum of disorders. The fear was the honest one. Biology has no clean equivalent for the Parkinson's and Alzheimer's labels, the line between them is porous, our brains don't respect it. Nearly eighty percent of people who die with Parkinson's have enough beta-amyloid in their brains to also fit the criteria for Alzheimer's. The labels are clinical conveniences. The biology underneath is something else: many processes, many pathways, one umbrella word.

Julian Lo, a retired pharmaceutical executive who became a Parkinson's researcher by necessity when his wife was diagnosed, put it more vividly: Parkinson's is like being hit by a shotgun; no two people have the same wounds.

The edges.

If the label were real, its edges would hold. They don't. The purest case is dementia with Lewy bodies versus Parkinson's disease dementia. Same Lewy pathology. But if dementia appears within a year of parkinsonism, it's called dementia with Lewy bodies; if parkinsonism comes first by more than a year, it's called Parkinson's disease dementia. The boundary is a calendar, not biology. An administrative rule decides which disease you have.

The edges blur in the clinic, too. Some people diagnosed with Parkinson's have normal dopamine scans, SWEDD, scans without evidence of dopaminergic deficit. Some people diagnosed with Parkinson's turn out to have multiple system atrophy, or progressive supranuclear palsy, different diseases that wear Parkinson's clothes in the early years. The rest of the boundary cases get a clause each: vascular parkinsonism, drug-induced parkinsonism, essential tremor that looks like tremor-dominant Parkinson's, REM sleep behavior disorder that may or may not become anything. The umbrella leaks in every direction.

A colleague once asked me whether Parkinson's is even a movement disorder. I said no: it's a communication disorder, a break in the circuitry, a dysfunction of the electrical currents that drive ambition, desire, motivation, hunger, satiation. Calling it a movement disorder doesn't do justice to what it does.

And then there is the symptom count. Parkinson's UK puts it at more than forty symptoms, tremor and rigidity and slowness, yes, but also loss of smell, constipation, sleep disorders, depression, anxiety, pain, apathy, drooling, freezing, falls. And from my own experience, each symptom in each person seems to evolve at its own rate, unique to that individual, which further complicates any

attempt to treat them, because there is no single course of the disease to aim at. Forty-plus symptoms under one label, each on its own timeline. At my first World Parkinson Congress in Portland in 2016, I walked the halls and saw a thousand different diseases. That doesn't prove the label is false, one disease can have many symptoms. But it tells you the label is doing an enormous amount of work.

The biology.

Kelvin Luk, who studies synuclein strains, told me in 2018 that there are "at least half-a-dozen different diseases that we call synucleinopathies," and that theoretically there could be hundreds of different strains. One protein, many strains, many diseases. The clumps are not one thing. They are a family of things, wearing one name.

The staging doesn't hold either. In a 2026 autopsy study of 61 confirmed cases, Braak stage, the famous six-stage map of synuclein spread, did not correlate with how advanced the disease was clinically, how long it had lasted, age at death, or brain weight. Co-pathologies were the rule, not the exception. The map that was supposed to show the disease marching through the brain in order doesn't predict how sick a person was, how long they were sick, or what else was in their brain. The stages are a story. The brains are something messier.

Genetics tells the same story. Ziv Gan-Or's work puts heritability around 30%, most of the risk is not genetic. The genetic slice itself fragments: LRRK2, GBA, PINK1, Parkin, and more, each a potential different mechanism, all under the same label. Back in 2019, *Brain Fables* counted 72 therapies with presumed disease-modifying effects, and only 8 targeted a defined subset. The field was aiming at the umbrella, not at anything under it. Five years later, the 2024 pipeline survey counted 136 active trials, 60 of them disease modifying, and only three disease modifying treatments in Phase 3.

My own history fits the sequence. I carry a GBA mutation. I had childhood migraines, an Epstein-Barr infection in my late teens, bouts of irritable bowel syndrome. My hypothesis, and it is a hypothesis, not a proven chain, is that those hits led my T and B cells into the basal ganglia, damaging the dopamine circuitry. One case proves nothing. That is why the 2022 piece ended with a call to collect more patient histories: patterns only emerge across many stories.

The trials.

This is where the umbrella does its damage. Biogen's anti-synuclein antibody failed. Sanofi's GBA-targeted drug failed. Each was a reasonable bet on one mechanism, and each was tested on a population defined by a label that contains many mechanisms. A drug that works on one disease under the umbrella will fail in a trial full of the others. The failure looks like a failed drug. It may be a failed population.

The newest exhibit is NOPARK, published in JAMA in October 2026. Four hundred and ten people with early Parkinson's, randomized to nicotinamide riboside, a form of vitamin B3 meant to raise NAD+, a molecule cells need to make energy, 500 milligrams twice daily for 52 weeks, or placebo. The result: UPDRS scores rose 2.45 points on the drug and fell 0.27 on placebo, an adjusted difference of 2.72 points favoring placebo. Non-motor burden worsened more on the drug. Four of five key secondary outcomes showed no difference. Fairness requires saying the gap was modest, below the usual clinically important threshold. NOPARK does not prove heterogeneity. But it is the rinse-and-repeat playbook in miniature: same premise, new molecule, same result.

Tony Lang asked the question this creates. With a limited number of eligible patients, how do you screen people for one drug or another? The trials compete for the same narrow slice of patients who fit their criteria, and the criteria are built on the label, not the biology. Multiple LRRK2-inhibitor trials can end up fishing in that same pool, each needing its own sub-subset matched. You cannot just enroll "Parkinson's." You have to enroll the right Parkinson's. And Clemens Scherzer's genetics program showed the scale of the problem, and a deeper fracture. A genome-wide survival study of 3,821 patients over 12 years found five progression loci, and they diverged from the known susceptibility loci: the genes that start the disease may largely differ from the genes that drive it forward. The authors concluded larger populations studied over time would be needed to find the rest.

Ziv Gan-Or, whose work put the heritability figure at around 30%, worries the problem runs one layer deeper still: even subtype-focused trials may fail, because they treat every variant inside the subtype as identical. Enroll all GBA carriers as "the GBA group," randomize, and one unbalanced draw can sink a drug that works. The umbrella doesn't just confuse the disease. It confuses the trial.

Alberto Espay gave me a better name for my own condition years ago: nigrostriatal degeneration. It names the network that is failing, not a disease no one can point to.

But the umbrella has one virtue, and it should be named. Levodopa works for most people under it, at least for a time, not because their diseases are the same, but because it replaces the dopamine their different diseases all end up depleting. DBS works the same way, for the selected patients who qualify: it modulates the shared circuit, not the diverse upstream causes. Lumping is fine for symptomatic treatment. Splitting is mandatory for anything that tries to slow progression. The umbrella fails as a research category. As a clinical category, a way to deliver treatments that act on the shared downstream damage, it has improved millions of lives, including mine.

The answer, in outline.

As Alberto puts it, we've learned a lot about Parkinson's disease, but we know next to nothing about

any individual living with it. The way out is not a better umbrella. It is to stop studying the umbrella and start studying what's under it, biology before labels, in a cohort built for exactly that. Chapter 21 tells that story. Here the point is simpler: if Parkinson's is not one disease, you cannot study it as one.

You cannot cure a label.

Chapter 13 — What We Measure

If the label is an umbrella, what do we measure? Chapter 12 left that hanging. This chapter answers it, or rather, the field has been answering it badly for decades.

Jon Palfreman saw it early. Palfreman is a documentary filmmaker who was diagnosed with Parkinson's while researching his book *Brain Storms*, and when I interviewed him in 2018 he laid out the problem plainly. To test a drug meant to slow Parkinson's, you recruit a reasonably similar group of people in early stages, and you track them for three to five years using the Unified Parkinson's Disease Rating Scale, the UPDRS. He described that scale as crude and highly variable, and said that changes of two or three points on it are treated as evidence that a treatment works. And then he added the line that has stayed with me: even if you had the cure, it would be very difficult to prove it works.

That is not a complaint about effort. It is a complaint about the ruler.

The ruler.

The UPDRS, now the MDS-UPDRS, the Movement Disorder Society's version, is the field's gold standard. It is a questionnaire and an exam. A clinician watches you move, asks you questions, and produces a score in points. It was designed in the 1980s. It measures how you look at a single clinic visit, on a single day, at a single hour.

That is the first problem: a snapshot. Parkinson's symptoms fluctuate with fatigue, stress, and the timing of your last dose of medication. One visit catches one moment in a moving disease. The trajectory is long: diagnosis, a bump from levodopa, decline as the drug loses power and side effects mount, deep brain stimulation as the last line of defense for those who qualify, then motor and non-motor symptoms no one can properly manage. The second problem is deeper: the scale measures symptoms, not neurons. It can tell you whether someone's tremor looks better this month. It cannot tell you whether their neurons are dying more slowly. A drug that slowed neurodegeneration by twenty or thirty percent might not separate from placebo on the UPDRS at all: the scale is a filter that mainly catches large, obvious symptomatic change, and lets slow preservation slip through.

The record shows what that filter has cost. As Chapter 11 showed, 85.1% of trials failed. The new molecules the system is built to produce, novel therapies, reached approval 21.4% of the time. Repurposed drugs, old drugs tried for a new purpose, only 6.7%. The system is good at the thing it was built to do, and it still fails most of the time. Those numbers are not just a story about bad biology. They are a story about a measurement system that cannot see what it claims to be looking for.

Paul Cannon made the same point from inside the research world. Diagnosed with Parkinson's in early 2011, he went on to run Parkinson's research at 23andMe, and his version was that even when we have objective biomarkers, the real test is still whether the patient feels and functions better. That is the right standard, and the UPDRS is a poor way of meeting it, because it substitutes a clinician's snapshot for a patient's life.

As my adaptive DBS was being switched on in November 2021, I made the point plainer to one of the engineers who built the technology. Symptoms are my disease, I told him. I can't feel my proteins aggregating.

I wrote about this mismatch in 2019. Pharma's definition of success is a drug that slows degeneration by about twenty percent in a Phase 3 trial, enough to beat placebo. Success, then, means a stock-price jump, bonuses, champagne in company offices. Patients would welcome that drug. But their celebration would be more subdued, because their definition of success is different: halting the decline, or reversing it. The threshold serves pharma's need to beat placebo. It does not serve patients' need to halt the decline. And the first successes will most likely help only a small subset, which a ruler built on averages is designed to miss. As the epidemiologist Karen Raphael, who has lived with Parkinson's herself for years, puts it, the trial's "average" patient is a statistical construct, not an empirical reality. The ruler is calibrated to someone who doesn't exist.

There is a reason the system works this way, and it is worth stating fairly. Disease-pathway drugs need a visible symptomatic effect within about a year, because the trial measures are symptomatic and because patients need to be able to tell whether a drug is working. That is the logic that built the ruler. It is also a trap: a drug that works slowly, at the level of the disease rather than the symptom, is invisible to the very instrument meant to detect it. And there is a second trap underneath the first. Restoring function is measurable: you can watch someone move better. Preventing loss is a counterfactual. You cannot measure what did not happen, which is why a trial designed to prove prevention has to run for years and still may show nothing.

Underneath the ruler sits a harder problem, and honesty requires naming it: some of this elusiveness is not the field's fault. By the time Parkinson's announces itself, a tremor, a dragging foot, the disease has usually been at work for years, and much of the damage is already done. Nearly everything the field calls disease-modifying aims only to slow what remains from getting worse; it does not promise to rebuild what is gone. Patients hear "cure" and picture reversal. What is actually on offer, even in the best case, is a slower decline.

The one family of approaches that might restore lost function, replacing the cells themselves, still has to answer whether new cells can survive in a brain that killed the old ones, and whether the degeneration would simply continue around them.

Prevention would be better than all of it, and prevention runs into a wall of its own. The disease can smoulder for a decade or more before diagnosis, and its earliest signs, constipation, a lost sense of smell, acting out dreams, a subtly changing gait, look exactly like ordinary aging. Genetics names only a subset of the people at risk, and carrying even a major risk variant does not say whether the disease will come, let alone when. A prevention trial needs people who will actually develop meaningful impairment within the next few years, and finding them, reliably, cheaply, at scale, is a problem the field has not solved.

PPMI and the Fox Foundation's Path to Prevention platform are genuine attempts at exactly that problem, registries built to find people early and learn who converts, and they deserve credit as attempts, even from me. The biology is extraordinarily hard; I have never believed otherwise. But hard biology is a reason to build better instruments and ask better questions. It is not a reason the same instruments and the same questions should go unexamined for thirty years.

The ruler also decides who counts. The trials that use it run in a narrow band of the world: there is effectively no mid- or late-stage drug development across South and Central Asia, Africa, or South America, which means the genetically diverse populations who might respond differently are simply not measured. And it decides what counts. The dominant theory says the disease is toxic protein piling up, so the assays reward clearing the piles: a loop that confirms the theory by construction, whether or not the theory is right.

Some say we need to crawl before we can walk. Fine, but keep the end goal in mind.

The stress test.

In March 2026 I wrote that the next twelve months would be a stress test for precision medicine: the field was finally testing whether targeting specific genetic pathways produces real benefit in people. The results are in now, and both bellwethers failed.

LUMA tested BIIB122, a drug that blocks LRRK2, a protein made by a gene linked to Parkinson's, in 648 people with early Parkinson's. The primary endpoint was time to confirmed worsening: a rise of six points or more on the UPDRS. The result was a hazard ratio of 1.04, essentially no difference from placebo. Secondary endpoints showed no benefit either. Biogen and Denali discontinued the drug for Parkinson's without a known genetic cause.

Here is the part that matters for this chapter: the drug did what it was designed to do. Blood tests showed more than 90% inhibition of LRRK2. A marker of LRRK2 activity in spinal fluid fell by about 30%. The biochemistry moved. The clinical score did not.

ACTIVATE tested BIA 28-6156, a drug meant to boost GCase, an enzyme that recycles waste inside

cells, in 271 people with Parkinson's who carry GBA gene variants. The result: a favourable safety profile, but no efficacy in slowing disease progression at the doses studied. Bial closed the program.

Fairness requires holding two readings of these failures at once. One is that the biology was wrong: LRRK2 inhibition does not slow Parkinson's without a known genetic cause, and boosting GCase does not either, and the trials correctly said so. The other is that the ruler could not detect a real effect: the drugs may have slowed something the UPDRS cannot see. The chapter's point is not that the second reading is right. It is that the system cannot tell the two apart, and a system that cannot distinguish a failed drug from a failed ruler will keep producing the same result, at the same cost, indefinitely. And notice which of the two readings the system reaches for. Faced with a failed drug or a failed ruler, it funds the ruler's replacement: more granular measures, earlier patients, better molecules, anything but a better idea. Sometimes a drug does fail. It is replaced by another drug under the same hypothesis. The biggest ideas are too good to replace. A belief that every failure only refines has arranged never to be wrong.

The physics problem.

This is a physics problem, yet all we have to solve it are the tools of biologists. No wonder we are busy counting cells.

My friend Lee Smolin, a theoretical physicist who has Parkinson's himself, asks a version of it that no biologist's tool can touch: why does the degeneration begin on one side of the brain and stay lopsided for years, a symmetry broken and never repaired? He has put the question to every doctor who would listen. Nobody has answered him.

Consider what the biologist's toolkit actually is: the microscope, the stain, the sequencer, the knockout mouse. Exquisite instruments: for biology. They tell you what the parts are, where the parts sit, and what happens when you remove one. They were built for a science of things.

But the brain is not a thing problem. It is a process problem, a flow problem. A hundred billion cells holding voltage gradients against entropy, trading information at kilohertz speeds, balanced on thermodynamic knife-edges. Nothing in the biologist's toolkit measures a voltage gradient decaying. Nothing measures a bit-rate. The tools operate at the wrong layer of abstraction. It is like trying to debug software by counting transistors: you can be very busy, very precise, and you will never find the bug.

So we count cells. We stain the dead ones, photograph the clumps, sequence the code of the broken machine, and mistake the inventory for understanding. An entire field performing an exquisitely detailed autopsy on a problem that is still alive.

The tools that would work belong to the electrical engineer: the oscilloscope, the signal analyzer, the circuit model. Measure the voltage. Measure the noise. Find where the signal decays, and tune it back. We know this works, because the single most transformative thing that ever happened to my brain was done with an engineer's tool, a wire, a battery, and a current, tuned like a radio.

Palfreman had seen the other half of this in 2018. He said biology is more complicated than physics, and that sequencing the genome had not produced the medical revolution people expected. The parts list was not enough. He was right, and the reason is that the parts list was never the right kind of knowledge. What we needed was the manual for the machine the parts make up.

The biophysics answer.

The argument for that manual arrived, fittingly, as a debate. I had arranged for Alberto Espay to speak to PD-Connect, a San Francisco-area patient group, expecting an update on the synuclein idea from *Brain Fables*. Instead it became an argument between Espay and two of his colleagues, Malu Tansey and Matt Farrer, who challenged him openly, to their credit. Espay argued for biophysical phase transitions: proteins shifting between states, like water freezing. Farrer pushed back, saying that for people with SNCA duplication or triplication, extra copies of the synuclein gene, you don't need biophysics to explain the disease, because the genetic relationship is direct. He was right about the gene dosage in those cases, and he agreed that a trial to lower expression in those people, early, urgently needs to happen. But gene dosage did not settle what was happening to the protein. The debate was not about who was right. It was about which layer the explanation lives at.

I came out of it with a framework, stated plainly. Two of its ideas were already on the table in that argument. The first is emergence: the brain's behaviour emerges from billions of interacting parts, and systems like that can undergo phase transitions, sudden shifts, tipping points, the way water turns to ice, so biophysics can model the tipping point before the system collapses, instead of merely cleaning up the aggregates afterward. The second is that genes are not proteins. Genes are static code; proteins are dynamic execution, modified by their environment, changing moment to moment, so sequencing alone will not explain neurodegenerative disease, because protein behaviour has to be understood through thermodynamics, the physics of how things fold, move, and settle.

Kariem Ezzat put the paradox to me plainly. An extra copy of a gene is usually read as simple overproduction. But proteins do not have to obey the gene's arithmetic. Push more protein across its solubility threshold and more of it can partition into aggregates; the amount left soluble, native and available to work can fall even as production rises. Clinical measurements complicate the slogan in the same direction: patients with SNCA duplication and extensive Lewy pathology have shown low levels of α-synuclein in spinal fluid, much as Aβ42 falls in Alzheimer's spinal fluid as it is deposited in the brain. Those measurements do not capture every pool of protein, and they do not erase the

genetic dosage effect. They expose the layer problem. Gain at the level of the gene can become loss at the level of function. Read duplication only as "too much protein," and the possibility that the working protein is being depleted never enters the room.

The rest of the framework is about what kind of system the brain is. It is an electrical circuit: neurons are biological batteries, their signals depend on voltage gradients and resistance, and disease can be reframed as circuit failure and signal decay. It is also an information system fighting noise and entropy, the universe's tendency toward disorder, to keep its signals clean; a measure like signal-to-noise ratio, borrowed from information theory, could give a far more objective and sensitive diagnostic than a questionnaire score. That answers the endpoints problem directly: measure the signal, not the snapshot. And the system runs on energy and scale. The brain uses about twenty percent of the body's calories despite being about two percent of its weight, and its cells hold themselves together by spending that energy. Parkinson's can be seen as a collapse of energy flow, including the failure to maintain the voltage gradients inside mitochondria, the cell's power plants. Larger brains, meanwhile, need thicker, more space- and power-hungry axons, the long wires neurons use to talk to each other, while heat dissipation and signal delay impose a physical ceiling.

The Monster Truck analogy puts the relationship in one image. Mendelian genetics, the rare, powerful single-gene mutations, is the truck that accelerates Parkinson's. Physics is the road it drives on. Studying only the truck is like analyzing engine parts to explain a pile-up caused by an icy road. Physics can predict when the road will ice over; biology only tells you the truck has a heater. The numbers sharpen the point: extra copies of the SNCA gene carry a risk more than ten times background, while the most common SNCA risk variant barely moves the needle, at about 1.4. Same gene, two different worlds, and only the physics layer explains why.

Not everyone around me buys the vocabulary. When I surveyed four experts on oscillopathies back in 2021, Alfonso Fasano, my own clinician, a man whose living is modulating these networks, called the term "a fancier term to indicate a brain network problem, pretty obvious at this point," and added: "It won't change how we approach PD." Ro'ee Gilron, who helped build adaptive DBS, was nearly as cautious: the term was not accepted yet, and the evidence linking oscillations to symptoms was correlational. I keep their demurrals attached to the framework on purpose. A lens is not a law.

The SNCA story itself carries a warning about how the field reads its own data. Gene triplication increases synuclein production and causes Parkinson's, yet the common risk variants for ordinary Parkinson's seemed to be associated with *lower* synuclein expression, a paradox Farrer had wrestled with for twenty-five years. One proposed explanation was that high protein levels drive rapid clumping, locking protein into solid masses and removing it from the soluble pool being measured, so the low measurements were misleading. But when Farrer, Kariem Ezzat, and I re-examined the data together, Farrer's lab data plus the public Braineac and GTEx datasets, the paradox dissolved in

the data itself: the susceptibility variants were not correlated with lower gene expression after all. The lesson is not that biophysics explained the paradox. It is that the field's measurements were producing a puzzle that was never really there, which is what happens when you measure the wrong layer.

In February 2026, the network view stopped being a framework and became a measurement. A large team publishing in Nature mapped the circuitry of hundreds of people with Parkinson's and found that the subcortical structures the disease damages are wired most strongly not to the brain's movement regions but to a network called the SCAN, a system that binds action to the state of the whole body, and that in Parkinson's that network runs hyperconnected: too loud. Levodopa quieted it. So did DBS. And in a small randomized trial, aiming non-invasive stimulation at the SCAN instead of at the classical motor strip roughly doubled the symptom relief. The treatments that work were never really fixing a spot. They were retuning a network. The field just hadn't drawn the map.

What to measure instead.

At the MJFF Therapeutics Conference in October 2026, Erez Eitan of NeuroDex wrote up what he'd heard with unusual candor. The field, he said, still doesn't know whether alpha-synuclein is a driving cause, a propagating agent, or a consequence. Patients differ in what drives their disease. "If patients differ in what drives their disease, how do we tell them apart?" His answer was more biomarkers: at NeuroDex, the tiny parcels neurons shed into the blood, which give a window into living neurons and capture cellular function. The candor is the point: a participant stating the field's open questions plainly. But the answer is the same apparatus, a better ruler.

The answer the framework points to is not a better questionnaire. It is a different kind of measurement altogether: diagnostics that measure a neural circuit's bit-rate, how much information it carries per second, and the voltage gradients inside mitochondria, instead of only hunting for proteins. Continuous monitoring from wearables, the kind Rune Labs was already building when I wrote about it in 2023, replaces the snapshot with a stream: thousands of real-world data points for tremor, gait, and falls, gathered where people actually live. The infrastructure to bypass the UPDRS already exists at scale. What has been missing is the willingness to ask regulators to let it count.

Riggare has been making the same argument from the patient's side for years: every prescription is already an unmonitored N-of-1 experiment. Her proposal, a "phase 4" that follows real-world drug use with trial-grade rigor, has been on the table since 2018. The method exists. The willingness doesn't.

There is a third thing the willingness has to build, and it exposes how loosely the field uses its favorite word. Every institution now promises precision medicine, therapy tailored to the individual.

But nobody has built the ruler for it. There is no agreed measure of how personalized a therapy actually is: nothing that distinguishes a treatment tuned parameter by parameter to one nervous system from a slogan with a biomarker attached. Until that ruler exists, "precision medicine" is an unfalsifiable promise. Every institution can announce the transition; none can be proven not to have arrived. So we will keep hearing about the urgent necessity of the paradigm shift, in ever more urgent and ever vaguer terms, because there is no instrument that could show it hasn't happened.

That willingness has to come with two more changes. The first is pre-competitive data-sharing: collaboration that does not evaporate the moment a molecule enters Phase 2 and intellectual property takes over. The second is longitudinal human datasets, following real people over years, combining device data with biochemical data, the way the Cincinnati Cohort is designed to do. Science, I wrote in 2023, is a collection of agreed stories, and trials are pharma's main test of which stories to believe. The stories the field agreed on, one disease, one ruler, one clearance theory, have had their test. The results are in. It is time to agree on better ones.

Knowing what to measure is one thing. Deciding what to do with your own brain, with the tools that exist now, is another.

Chapter 14 — The Decision

In January 2021, I sat down to decide whether to let someone drill into my skull and put a machine in my brain.

There is no equation for a decision like that. No formula that takes your symptoms, your age, your brain, your life, and outputs an answer. The field that can map a protein's folding has no method for the most important decision a patient ever makes. That absence is the subject of this chapter.

It was, as I wrote at the time, the most important decision I might ever have to make about myself. Not because brain surgery is dramatic, though it is, but because the decision couldn't be undone, couldn't be outsourced, and couldn't be made by anyone but me. No doctor could make it for me. No paper could make it for me: none exists that could. No one else would live with the consequences.

The machine on offer wasn't ordinary DBS. It was adaptive, a device that reads the brain's signals and adjusts its own stimulation in response. And the question at the heart of it was stranger than the surgery itself: How is the brain, which is itself an ever-adapting system, going to adapt to a device that is constantly adapting to it?

That's the ouroboros, the snake eating its own tail. A brain that rewires itself, fitted with a device that rewires itself in response. I was being asked to sign up for a loop with no exit, and to do it on the basis of information that was, by the field's own admission, incomplete.

I was thirty-six. Seven years and three months post-diagnosis. And I had four options.

Deep brain stimulation, the adaptive kind. Electrodes implanted in the brain, in my case, the subthalamic nucleus, a small structure deep inside, about six millimetres across, connected by wires under the skin to a battery pack in the chest. The electrodes send electrical pulses that change how the brain's circuits fire. The settings can be adjusted, the device can be switched off, the whole thing can be removed. It is the oldest and best-studied of the four options, and the only one that would have been available to me when I was diagnosed. It does not stop the disease. It manages the symptoms, and, as I would learn, it manages them by rewiring the circuits that make you who you are. The risks are those of brain surgery: bleeding, infection, stroke, plus the subtler ones the consent forms list in smaller print: speech, mood, thinking. And the experience counted: by one count, more than 150,000 people had already had it when I was deciding, the figure has since passed 250,000, and I was not going to be anyone's prototype.

Cell replacement. Put new dopamine-producing cells into the brain to replace the ones the disease killed. The idea is the most intuitively appealing of the four: restore what's lost, rather than masking what's missing. The history is the least reassuring. The early trials used fetal cells, with mixed results and real ethical problems. The newer versions use stem-cell-derived neurons, and the field's own experts, Kordower, Loring, Studer, Björklund, Barker, Freed, surveyed in 2018, were candid that the approach was still experimental: promising biology, unproven in people, with risks that include surgery, runaway growth, and dyskinesia caused by the graft itself. The promise is restoration. The reality, in 2021, was: not yet.

Focused ultrasound. No incision at all. Focused beams of ultrasound, guided by MRI, burn a small, precise lesion in the brain, destroying the tissue that generates the tremor or the rigidity. The appeal is obvious: no drill, no implant, no battery. The catch is equally obvious: a lesion is permanent. You can't adjust it, switch it off, or take it out. And the target matters enormously, which is where I should own an error. When I first wrote about these options, I clumped focused ultrasound in with a lot of pseudoscience, and I confused PTT with pallidotomy and thalamotomy, near-identical names for lesions in different places. A reader, Julian Lo, corrected me. The correction matters twice over: first, because the details matter when the target is your brain; second, because even the hyper-informed patient gets them wrong. The information landscape is a minefield, and I was walking it with a map I'd drawn myself.

Gene therapy. Deliver genes into the brain, usually via a harmless virus, to make the brain produce something it's missing: an enzyme that helps levodopa work better, or a growth factor meant to protect the remaining neurons. One-time, irreversible, earliest stage of the four. The science is elegant. The evidence, in 2021, was thin.

Four options. Four different bets on the same brain.

Here is what nobody tells you about knowing a lot: it makes the decision harder, not easier.

"I actually find myself a bit paralyzed by all the information I have." I wrote that sentence in January 2021, and it was the truest sentence in the piece. A patient who knows less decides faster, not because the decision is easier, but because they can't see how hard it is. I could see it. I knew every option's failure modes, every trial's caveats, every expert's disagreement with every other expert. Knowledge didn't resolve the decision. It revealed how unresolvable it was.

And the decision was a privilege. That sounds strange to say about brain surgery, but it's true: only one of the four options would have been available to me when I was diagnosed. Seven years had

produced three new ones that didn't exist then. Progress is real, just slow, and unevenly distributed. Much of the world still doesn't even have access to the basic medications developed sixty years ago. Most patients don't get to choose among four brain surgeries. Most patients can't get levodopa.

So the question I ended that piece with was the real one: how can we develop a method to weigh each therapy's advantages and disadvantages against each other for each patient?

There is still no such method, no equation, and no real attempt at one, that can guide a patient through this all-important decision. Though maybe it's coming. That absence is an indictment of the field: thousands of papers on the biology, and no real attempt at the decision itself. That question was about the irreversible choices. For the reversible ones, the experiments patients run every day, part of an answer already exists: the N-of-1 trial Riggare has been arguing for since 2018, waiting for trial-grade rigor. There is no patient guide to DBS, no manual that tells you what you're going to go through.

A consent form is a legal document. It lists what can go wrong: hemorrhage, infection, stroke, speech problems, mood changes. It does not, it cannot, tell you what it will feel like to have your brain rewired, or what you will trade away, or who you will be on the other side of it. Those are not risks you can list. They are a life you have to live. The form I signed didn't contain them. No form could. That is not a complaint about the form. It is the point: the decision that matters most is the one no document can make for you.

I turned to the patients who had come before me, my fellow adventurers into the brain. They knew things no consent form contained. It is an indictment of society that our health systems don't recognize the value they have to offer.

The accumulation began the first time I stepped into Fasano's office. He drew a neuron for me, on paper, by hand, and labelled the parts: the axon, the dendrite, the synapse, the nucleus. A diagram any textbook could have given me. But a textbook wouldn't have taken the time.

What that drawing started to build was trust. Not trust in a procedure, or a device, or a paper: trust in a person. That he would guide me, and give me the time I needed to understand what was happening to me then, and what would happen in the future.

Two years earlier, I had spent four hours in Hagai Bergman's office at Hadassah Medical Center in

Jerusalem, a private lecture on closed-loop deep brain stimulation. I didn't understand everything he said. But I had no idea at the time that he was painting my future.

I had three requirements for going through with it. A good surgeon, Suneil Kalia at Toronto Western, someone I was comfortable with, who I trusted to make decisions on my behalf. A programmer and physician who knew me, who I trusted implicitly. And a family environment to come home to, someone who could do everything for me if I couldn't do it for myself. If I hadn't had all three, I wouldn't have gone through with it.

I interviewed people who had made the decision before me, and they gave me the honest picture. Fasano himself, in 2017, had warned me that DBS is imperfect: it jams overactive circuits rather than stimulating them, most people improve but often lose other motor skills, and results can be unpredictable because the circuits aren't fully understood. Lisa Vanderburg told me her husband Pete's story: the medications maxing out, his reluctance about anyone messing with his head, her persuasion, a run-up she called pure torture, and well worth it, a switch-on that left him taller, straighter, younger, and then, years later, the disease progressing anyway. Paul Cannon, who had decided on DBS himself in 2018, walked me through his calculus: the fluctuations despite a good response to Sinemet, timing the surgery to avoid infection, the worry that the stimulator can be changed but the electrodes are for life, and the trade-off that DBS usually excludes you from trials.

The decision accumulated from there, through years of correspondence, of questions asked and answered, of a research tour and a collaboration, until, on March 22, 2021, I wrote to him: "I think I am ready. Would like to go ahead and book my DBS surgery now for the percept device with Suneil Kalia." That was not the moment I decided. That was the moment I said it. Within minutes he replied: "Leave it with me, do you want to be part of the ADAPT trial too?" I did.

And the decision was never just about me. On April 2, I wrote to him again, asking how to extract the maximum scientific value from the procedure. Could the neurons from my outer cortex be biopsied, preserved, studied in as much detail as possible? I wanted to show the ethics board I understood the risks, and to sign off on preserving the neurons. I even offered to speak to the ethics council directly. Part of it was curiosity. I was excited to be a living, breathing experiment. I was not a passive recipient of a surgery. I was a partner in it.

I was the first patient enrolled in the ADAPT trial in Canada. I was proud of that, and I felt guilty about it, because the trial had pushed me to the front of a surgical line full of people just as sick as I was, who would keep waiting. Both things were true. I didn't resolve them. I just carried them into the operating room with me.

That is how the decision was made. Not in a moment. Not by an equation: there is none. Not by a

paper: none exists that could. It accumulated, moment by moment, out of trust: in Fasano, in the patients who had gone before me, in my own growing understanding of what I was agreeing to. The form I signed at the end was the last step, not the first.

I didn't get DBS because I thought it would cure me. I got it because it would let me live better now. That was the acceptance: not waiting for the fix, but taking the life I had and making it better.

Going into it, I felt at peace with the decision.

I decided. The surgery, and everything that came after it, belongs to the next chapter.

Chapter 15 — The Honeymoon

Before surgery, I had about two hours a day when I could function, the rest was spent riding the On/Off roller-coaster between flailing (dyskinesia) and freezing (bradykinesia). I hadn't driven in a year. I kept Cinderella hours: anything past ten at night was off limits.

I told the full story of the surgery in *Reprogramming the Brain*. Here is the short version.

On June 1, 2021, they drilled the leads in. I was awake for the entire four-hour procedure. The most painful part was the freezing of the scalp, a dozen needles, so I wouldn't feel anything after. A 1.5-millimetre electrode went 10 centimetres deep into a 6-millimetre target in my subthalamic nucleus, the STN, a small structure that helps control movement.

Then they played the microelectrode recording aloud. The tip records individual neurons as the electrode advances, and the neurons' firing comes through a speaker: the team uses the pattern to confirm the electrode is in the right place. My brain was speaking to me. When the electrode hit the sweet spot of the STN, the sound went pitch-perfect. I tapped my fingers together, trying to manipulate it in real time. When they tested the stimulation on the left side, no medication since before surgery, my finger-tapping and wrist-turning went fluid. I felt euphoric.

But by the second side, the other half of my brain, the novelty had worn off. Hours in, the frame pressing into my skull, nausea building, a shearing headache. I wanted it over. I don't want to call it a religious experience. But in some ways, it was mystical.

The day after the holes were drilled, I felt ecstatic. My hands and feet were steady. My stride was longer. The On/Off cycle was nearly gone. For one day, the sine wave was flat, no fluctuations at all. It felt like I had travelled back in time to before my diagnosis.

On June 3, they put in the battery and the wiring: a pacemaker-like device under the skin above my right pectoral, with wires fish-hooked and tunnelled under the skin down my neck, connecting the leads to the battery.

Phase two brought constant pain when I moved my right arm. Sent home, I worried something had gone wrong, my neck was stiff, my head was swelling. I was told to be patient. This was normal.

My surgeon told me not to touch, shower, or apply any cream to the wounds. Just let biology heal. The incision healed into a ridge, like a small mountain range across my scalp, numb to my own touch, and I could feel the wire under my skin all the way down to the battery; when the dyskinesia thrashed me, it pulled. Staple removal was more painful than I expected, and left me feeling as

though my brain was oozing out of my skull. Programming was still weeks away, and could take up to six months. I had heard of people needing to redo the surgery, losing the ability to speak properly. I felt optimistic anyway. Excited. Curious.

Patience is a virtue, they say. I wondered if "they" ever had DBS.

The first programming session was not a light switch. It was a calibration.

I have a short video of it. A clinical exam room. Dr. Fasano in a white coat holding a tablet. I walk toward the camera, away from it, turn. He stands behind me, hands on my shoulders, and pulls me backward to test my balance. I sit while he presses buttons. I stand and walk again, a little more confidently this time.

People imagine the stimulation feels like the medication. It doesn't. Levodopa, in its good years, had felt like a wave, a mild euphoria; I remember walking down Queen Street suddenly chatting with everyone. Stimulation felt like a constant hum, as if something else was driving me from within.

By August, my days were beginning to be a bit more predictable. It was a quiet miracle: no more wild On/Off fluctuations, no more worrying about dyskinesia or rigidity, no more carrying pills everywhere. DBS had done that before the adaptive settings were even turned on. Part of my attention had always been taken up by the disease, always partially distracted by it. Now, for stretches, I didn't think about Parkinson's at all.

Espay clarified what I had. My form, he said, was "pure nigrostriatal," the degeneration was concentrated in the nigrostriatal pathway, the circuit that carries dopamine from the substantia nigra to the striatum, and unlikely to spread to non-motor regions. It didn't mean I was cured. It meant I knew which type of Parkinson's I had.

By August I was taking it further, in my own head: if the degeneration lived in one circuit, and a machine could compensate for that circuit, then in the way that mattered I didn't have Parkinson's at all, not the umbrella disease, anyway. Before the surgery I had given myself maybe fifteen good years. Now I gave myself thirty. I believed it entirely.

I knew how lucky that was. Most patients never learn their form. Most never get care like this. I had spent six years studying Parkinson's science and health systems, I lived near a leading hospital and team, and my retired parents could help my recovery. The gratitude was real, and so was the gap: I

got this because of where and when I lived, and because of what I had taught myself. Most get neither.

In November 2021, we turned on the adaptive settings. The device would now decide, moment by moment, how much stimulation to deliver to my subthalamic nucleus, based on the brain signals it was reading. An algorithm would run a part of my brain.

The results were pretty miraculous. After the June surgery and months of titration, I had been on six or seven Sinemet pills a day, cycling through severe dyskinesia then bradykinesia. Now, after months of slow titrating down, I was on less than one levodopa pill a day.

The mechanism, as I understood it, was about beta oscillations, rhythmic electrical activity in the brain that correlates with motor severity. When the oscillations desynchronised, the symptoms eased. The adaptive system was reading those rhythms and adjusting in real time.

This was not a cure. The underlying cell loss was presumably continuing. Some Parkinsonian days remained. There were side effects, difficulty swimming, trouble with bilateral control, neurological tics. But I was able to travel independently and spend a couple weeks living in a yurt in a California vineyard.

In January 2022, I ran into a word in a talk to ASAP network trainees: surgicogenomics, using a patient's genetic information to assess surgical outcomes: which patients should get which surgery, or where in the brain.

The example that stopped me was my own case: people with parkinsonism and a GBA mutation receiving STN DBS might decline faster cognitively. I carry a GBA mutation. My STN surgery had been just last June. That might have been helpful to know before the surgery.

It was a crack in the honeymoon, not a failure of the device, but a reminder that I had made a permanent decision with incomplete information. A large Italian study has since complicated the worry: GBA carriers do decline faster cognitively, but at the same rate whether or not they got DBS. The faster decline is driven by the gene, not the surgery.

In July 2022, I sat on a neuroethics panel at MIT Media Lab. Afterwards, two questions I had not raised kept coming back to me.

The first: what outcome data should patients see before consenting to an implant? Medtronic, Boston Scientific, and Abbott had implanted over 200,000 DBS devices by then, since FDA approval in 1997, and they own the outcome data. But there is no easily accessible repository, by device, by centre, by surgeon. Companies have little incentive to share. The burden falls on patients. Do patients not have a right to access that data?

The second: do we need ethicists on every trial? The same day, I tried a pair of Neurable headphones that detected differences between my DBS On and Off states, and even between adaptive and continuous settings. Something I had laughed off six months earlier. The device could read what my brain was doing. The question was who got to see that reading, and what they could do with it.

The honeymoon had given me a life back. It had also given me questions I had no answers to.

By October 2022, I was taking French classes. My new tutor could detect no signs of disease.

The numbers: my UPDRS, the standard Parkinson's rating scale, had fallen from over 50 before surgery to over 20 on continuous DBS to over 15 after the adaptive settings. My medication had fallen from 600 to 700 milligrams of levodopa a day, plus pramipexole and amantadine, to about 75. Dyskinesias were largely gone. My OFF periods were about 90 percent of normal. It had held steady for a year after turning the adaptive settings on.

So I wrote the sentence: adaptive DBS can functionally cure Parkinson's disease. I meant it with a strict definition, rewind to the pre-onset state, plus halt future progression, and I did not know if I myself was "cured." The durability was unknown. The underlying cause was unknown. The effect on neurodegeneration was unknown. DBS helped motor and sleep symptoms, not non-motor ones. And I had excellent care, a supportive home, and a team most patients will never get.

It was hype. It was also, for me, true. That is the tension the honeymoon lived in: the results were real, and they were not generalisable.

In March 2023, I listened back to a podcast interview and noticed my speech had changed. Word-finding was harder. The words came slower. I did not know if it was the Parkinson's or the DBS. Nobody really knows which.

Fasano had asked me: would you rather be able to walk or talk? The choice is not truly binary, and life with Parkinson's and DBS is about trade-offs. But if forced to choose, I chose walking. I'd told him before the surgery: I'd rather be able to walk and type than talk. I sympathised with people never given a choice.

This was the first crack that landed on me personally. Not a failure, a trade-off. The device that gave me my walk was taking something from my voice. I had made a living talking. The word-finding struggles were concerning, and likely to worsen. I asked for a Toronto-area speech pathologist recommendation. C'est la vie.

Exactly three years after two electrodes were implanted, I drove alone over 3,000 kilometres around northeastern North America, taking no symptom medication the entire trip.

I felt great. I had almost no bradykinesia, dyskinesia, or dystonia (involuntary muscle contractions). I felt I could live my life, for the most part, free of disease.

It was not perfect. Slight tremor. Occasional slurred speech. Wonkier gait and balance. A battery needing replacement about yearly. But it had taken a village to get me here: Fasano, Suneil Kalia, Alexandra Boogers, nurse practitioner Yu-Yan, who knew the programming better than anyone else in the clinic and cared about the person attached to it, the UHN and Medtronic teams, my parents. Each deserving of more praise than there are words for in this book. Suneil was my wonderfully understated neurosurgeon, the opposite in every way of the stereotype of his profession. Neurosurgeons often think of themselves as gods and carry the swagger to match; he does not. And the village had held.

The honeymoon was over. The marriage was not. The device was still there, still tuning, still trading walking for talking, still leaving questions unanswered. The miracle months had been real. So was everything that came after them.

Chapter 16 — The Blunt Instrument

Five years after they drilled holes through my skull, my neuropsychologists told me I was "still very much a poster child for adaptive Deep Brain Stimulation."

If you want to know what being a poster child actually looks like, come sit in Dr. Alfonso Fasano's exam room in July 2026.

My five-year clinical trial had finally ended. For the first time since the wires went in, Alfonso was unencumbered by a trial protocol and the impositions of a corporation looking over his shoulder. He was free to spin his artistry in me. To know where the boundaries of my adaptive algorithm's parameter space really sat, he had to stress-test my settings, which meant pushing me past the ranges where I was comfortable.

There is nothing else in human experience quite like being programmed. A few feet away, a doctor sits with a tablet, pressing buttons on a screen. With every incremental tap, you feel a tingling of electricity inside you as your nerves constrict your muscles one half of your body at a time, opposite the side of the brain being tuned. At one point during that session, the current hit a threshold and I jumped out of my chair, twirling around the room in a wild fit. A few moments later, another tap pinned me back to the chair, unable to speak, my right hand locked in place, clenched above my head.

Sitting there, catching my breath, I asked Alfonso how many of his colleagues he would trust to program his own DBS if he ever needed one.

I stayed in that chair because of ten years of trust, because I knew he would not let me walk out of his office feeling worse than when I walked in. And despite how terrifying the description above sounds, I should admit something that even I find strange: it feels good to get programmed.

It is not only Alfonso. Alexandra Boogers, a fellow at the clinic, once sat in that chair and, with a few taps of her tablet, carried me out of the body of a frail old man and back into something close to the body I had twelve years ago. I have a name for that gift: the soul doc, the programmer who gets you without your having to explain. Then her fellowship ended, she went home to Luxembourg, and the gift went with her. That is the arrangement's quiet fragility: the expertise that tunes you lives in people, and people leave.

There is theatre in it, too, and Alfonso doesn't hide it: he can fake it. He can mime pressing the buttons, change nothing at all, and the patient in the chair may still feel a difference, which is itself diagnostic information, one way programmers test whether a symptom is being driven by the circuit

or by expectation. The buttons are real. So is the belief. Programming works on both.

What Alfonso is shaping on that tablet, as he taps, has a clinical name: the VTA, or Volume of Tissue Activated. Put more plainly, it is a blob of electricity.

Around each active contact on the electrode, the current forms a three-dimensional field, rendered as a glowing shape on his screen. After years of visits, Alfonso and I know that my symptoms respond best when we activate the blobs around the two central contacts in each half of my brain. Together they form a shape that looks like a Russian nesting doll, with the blob around the bottom contact plumper than the one stacked above it.

That nesting doll is the state of the art in neuromodulation. It is also why deep brain stimulation remains a blunt instrument for a very fine disease.

Every session begins with an impedance check, a quick reset where the battery tests the circuit and briefly cuts the power. For a few seconds, I tense up, left without the life-giving electricity. (I learned how steep that drop is a few years ago when I had to spend thirty minutes inside an MRI tube with my stimulator switched off; watching the tremor and dystonia crawl right back into my limbs in that tube was a painful reminder of what my life would be without the wires.) Then the check finishes, the current comes back on, and something inside me releases. You might think it's dopamine, but it happens far too fast to be a chemical reaction. It is the circuit switching back on electrically, a rush of euphoria that washes through me, similar to what I feel when I crank up the speed on a treadmill and let the forced cadence take over. No one knows exactly how it works.

Start with the hardware and the geography. Pushing a 1.5-millimetre wire ten centimetres through living brain tissue damages what it passes through, kicking off neuroinflammatory pathways that do their own quiet harm, and over time, the tissue pushes back, the cells around the electrode gradually pulling away from a thing that shouts at them without listening. Then there is the geography: textbooks like to draw neat borders around the brain, the subthalamic nucleus controls movement; the amygdala processes fear and threat. The brain does not read our textbooks. Its structures are plastic and borderless. When a physician inflates a blob of electricity inside a six-millimetre target in the basal ganglia to quiet a tremor, the current doesn't stop at a dotted line. It spills into neighboring fibers that govern speech, balance, proprioception, mood, the circuitry of who you are.

In the honeymoon months of Chapter 15, trading a little clarity in my voice for the ability to walk without thinking felt like the bargain of a lifetime. Five years in, the tax is steeper.

Not too long ago, I could speak for hours on end. Now, there are days when I have trouble making myself understood at the kitchen table. That is the daily math of living with a blunt instrument.

The electricity is only half the equation. The goal of programming is never perfection; it is finding a "Goldilocks zone," a functional range where the current quiets the worst of the noise without slurring my words into soup, leaving me just enough bandwidth to manage the rest myself. And managing the rest is a full-time job. To hold onto the baseline the wires give me, eight to ten hours of sleep a night is non-negotiable. I do seventy minutes of heart-rate-elevated exercise damn near every single day. I joined a local boxing and balance class. I started studying languages again, not for fluency, but to force my brain into novel environments that keep its neuroplasticity alive. That is the ownership trap in my own regimen: the things that hold my baseline are the things nobody owns, so nobody tests them properly.

Even with all of that, the disease is still in the room. As I type these words, my left foot is tremoring, banging away against the floor beneath my desk. I still shuffle when I navigate tight spaces. And anxiety still has an ugly habit of stealing my sleep, surfacing in ways no electrical blob can fully suppress.

Still, for nearly five years, I was a vocal proponent of the adaptive version of this technology, the closed-loop system that reads my brain's signals and adjusts the current in real time. I co-wrote a book championing it.

Intellectual honesty requires telling you why I had to turn it off.

The first generation of adaptive DBS relies on reading a single signal, the beta frequency band in the local field potentials around the electrode, and adjusting a single parameter, amplitude, in response. When beta oscillations spike, the device ramps the current up; when beta quiets down, it dials the current back.

In a controlled clinic visit, that loop looks like the future. In the real world, the beta signal is volatile. Voluntary physical movement can wash it out. Medication cycles obscure it. Sometimes the signal simply drops out even as your motor symptoms are getting worse. And the algorithm has a critical vulnerability: when it fails to detect a strong enough beta signal to justify delivering power, it has a tendency to "rail low," dropping your stimulation to the lowest baseline setting in your predefined parameter space.

That baseline setting is fine when I am asleep and my body demands almost nothing. Navigating a day on my feet requires significantly more juice.

In the late summer of 2026, railing low became my reality. For weeks, my "smart" implant kept bottoming out my amplitude during my active hours. Instead of optimizing my brain, the adaptive algorithm was starving it of current. I became more bradykinetic than I had been in years. My range of motion shrank. My speech grew noticeably more slurred. I shuffled more, froze more, and took a

few falls.

At the end of August, I flew to Boston for a week of lab visits, already battling a two-week bout of medication-induced sleep deprivation, and spent the trip wobbling from lab to lab while my implant under-stimulated me.

What made the whole ordeal maddening was that I couldn't fix it myself. The current iteration of adaptive DBS gives the patient almost no control over the algorithm's parameters. Every adjustment, no matter how minor, ties you back to your clinic. For the patient, that means enduring physical strain while fretting over the logistics of booking an appointment just to tweak a setting. For specialized neurologists like Alfonso, it means schedules bogged down by routine troubleshooting. A high-tech therapy that requires a world-class specialist to manually rescue the algorithm isn't scalable.

There is, however, one saving grace to an adaptive DBS device. The late comedian Mitch Hedberg had a famous bit about escalators: an escalator can never break; it can only become stairs. Sorry for the convenience.

When the adaptive algorithm falters, the implant doesn't become useless. With a few taps, it can be switched back to the older, continuous DBS mode. I felt a pang of guilt when I did it, thinking of all the hours Alfonso and his team had poured into tuning my adaptive settings, but I knew they would agree that the point of the machine is for me to function. So in September 2026, I said goodbye to adaptive DBS and switched my brain back to continuous stimulation. It lacks the theoretical elegance of a closed loop, and it never bottoms out when I'm trying to cross a street.

Look closely at why the algorithm failed, and you will see Chapter 13's measurement trap playing out inside my own skull. The device was built to chase a single surrogate marker deep in the brain while ignoring the actual human being attached to it, though, to be fair (as Alfonso reminded me when I wrote about switching it off), adaptive DBS is capable of reading more than just beta frequencies, and clinicians are learning new tricks daily now that the technology is commercialized. The skepticism was there from the start, and from inside the field: Cameron McIntyre, one of the engineers behind the sensing technology, told me in 2021 that adaptive's real value might turn out to be smoothing the fluctuations rather than improving outcomes, and that knowing when and why to stimulate would take decades to disentangle. Yet right now, a wristwatch or a phone in my pocket can capture my gait, my balance, my tremor, and my slowness in the real world with far more fidelity than a single brainwave in my subthalamic nucleus. Until these "smart" implants integrate continuous, real-world behavioral data alongside brain signals, and trust patients with the controls to tune their own lives, they will keep losing sight of the patient, and the very people they were built to treat will keep overriding them.

Why we need something better is not a theoretical question. Even continuous DBS, the best tool we have for advanced Parkinson's, reaches only roughly two percent of the people who could benefit from it. It is invasive, it requires an elite clinical village to maintain, and its lack of specificity demands a lifetime of exhausting adjustments, hardware management, and battery replacements.

Ask David Ashford Jones, a patient in London I interviewed in 2021. His stimulator is a different brand from mine. His patient controller is an aging phone he was told would cost about £15,000 to replace. After his first programming session, his device sat switched off over a weekend before he discovered it. Same therapy, different country, different machine, different luck.

That sentence contains the argument this chapter has been circling: there is no "same therapy." DBS is spoken of as one thing, you "get DBS" the way you get a hip replacement, and it is nothing of the sort. The target is chosen per brain, subthalamic nucleus or globus pallidus, and the choice changes what the therapy does. The current's shape is sculpted per patient, per hemisphere, per symptom; my nesting doll is not Ashford Jones's nesting doll. The parameters are retuned over years of visits. This is what precision medicine was supposed to mean, and it already exists: a therapy adjusted, read and re-read, for one nervous system at a time, sitting inside a quarter of a million skulls. The field talks about precision medicine as a destination, a paradigm we must transition toward, while the most personalized therapy in neurology wears a single label. The label is the blunt part. "DBS" is one word the way "Parkinson's" is one disease: a convenience of language hiding the personalization the field claims to be chasing.

In Boston, I also saw what comes after the blunt instrument: the full story belongs to Chapter 22.

And yet, make no mistake: I would still choose to undergo DBS again.

Before the surgery, the slope of my decline was too steep to imagine living the life I live today. The electricity humming in my basal ganglia, paired with the discipline of my daily routine, bought me the ultimate luxury: bandwidth.

It is still the best therapy we have. I just do not believe it is the best we could have.

And the physical trade-offs, the slurred words at the kitchen table, the left foot banging on the floor, the algorithm railing low, were not even the steepest price the electricity extracted. The steepest price was what happened when that borderless blob of current didn't just move my muscles, or steal from my voice, but reached into the circuits that govern impulse, judgment, and identity.

A blunt instrument in the brain doesn't just tune the movement. Sometimes, it rewires the man.

Chapter 17 — Who Am I Now

A blunt instrument in the brain doesn't just tune the movement. Sometimes, it rewires the man.

So who is the man?

In October 2021, my uncle Felek came to watch a programming session. Fasano sat with his iPad, adjusting the settings, and with each stroke my tremor appeared or disappeared, on, off, on, off, like a light switch. Felek watched this for a while and then asked, in his own way, whether the person in the chair was still a man or had become something else. A machine with a man attached, or a man with a machine attached.

His own answer, after thinking it over, was that it wasn't, in principle, so different from taking a pill. A pill turns things on and off inside you too.

That scene has stayed with me because it asks the question in real time. A dial can switch parts of me on and off. So which parts are me?

I was also a little afraid of what I would do with the freedom. Parkinson's had taken it away, and if the switch gave it back, I had no idea how I would react. I hoped it was a problem I was going to have.

The wires alone hadn't changed me. Three weeks after the surgery, before any settings had been turned on, I was surprised by how ordinary I felt. I had been expecting more from having two metal rods shoved into my brain. You think of your brain as who you are; apparently you can run wires through it and still be yourself. Maybe the brain isn't as important as I thought it was. The changes, when they came, came from the current, not the metal.

A few weeks before that session, I sat with a psychiatrist for about two hours and walked out with a new diagnostic bumper sticker: hypomania, a milder form of mania. More curious than bothered, I did what I had done with the other clinical label I carry, and asked what precisely mania is.

The answer was familiar. Mania, like Parkinson's, doesn't refer to anything specific. It has no biological correlate. It is a hodgepodge of symptoms that we clump together for reasons that don't always make sense. One label for a bundle of things that may not belong together.

That bothered me less than the question underneath it. The adaptive settings were about to go on, I wrote about all of this the night before they were scheduled to start, though in the end the switch-on was pushed to November, and everyone around me was watching for one thing: whether the current

would tip me into a permanent manic state. Every time we had turned the dial up before, the behaviours people call manic got worse for a day, then settled back down over the next week. Settings that fluctuate all day long might not settle.

So I asked myself who I was doing this for, and why. I did not go through brain surgery so I could better fit into society. I went through it to get more control over my movements. If the current gave me back my hands and took my personality in exchange, was that a good trade? There would probably be a middle ground, movement mostly controlled, behaviour not tipped too far. But the trade-off was real, and it was mine to make.

And there was a harder question underneath that one. What if these episodes were not really driven by the stimulation at all? What if they were just me being me? The episodes had always gone in lock-step with my ability to move properly again. For eight years I had been losing ground to my own brand of neurodegeneration, and in those eight years I had grown more as a person and learned more about myself than in any other period of my life. Some people said that to find out who I really was, I just had to go back to who I was before the diagnosis. But that person was gone. How could I be expected to be him again, or to have anything a doctor would call a baseline personality?

Espay, who has known me before and after, put it this way: the personality is the same, just more Ben out there. The question is how to channel it. I felt it too, more childlike, senses heightened, more confident, and, I worried, slightly more arrogant. As if the surgery had given me an intuitive sense of how my brain works.

Andreas Horn trusted that intuition less. I had told him, that August, that one of the deeper contacts seemed to speed my thinking up while making my speech harder to get out, a gain and a cost on the same dial. Horn cautioned that stimulation can switch off some of the brain's checks and balances, and that the sense of thinking brilliantly can deceive: he compared it to a psychedelic insight, which looks considerably less smart the next morning. He proposed testing me blind, settings varied over days without my knowing, rather than going by my own report. It was a fair challenge. The instrument doing the reporting was the thing being rewired.

I didn't have an answer. I still don't. But the question got sharper the next spring.

In May 2022, I went in for the first adjustment to the adaptive settings in seven months: before the adaptive settings, I had been going in almost every two weeks. The settings were turned up, and then I was left alone in a dark doctor's office. I recorded voice notes for a couple of friends while I waited.

Part of me wanted to go outside and play in the sun. Part of me wanted to eat a whole pizza by myself, and then probably ice cream too. Part of me wanted to jump out of a window.

I didn't act on any of it. I had enough wherewithal not to, and I knew why: these thoughts were a temporary over-activation of a tiny part of my brain, and they weren't really me. I knew they could go away as soon as the doctor came back and pressed a few buttons. In the end I didn't even need that: over two hours, and after a meal, my brain adjusted itself and I felt more or less like the person I was before.

But I kept thinking: what if it had been permanent? What if my brain hadn't adjusted, and I hadn't been able to tell the doctor what I needed? Fasano knows me well enough that he probably would have known anyway. But what if he hadn't? What if I had been in someone else's care, someone who didn't know me well enough to see that I was no longer acting like myself? What if I had been older, in a wheelchair, unable to speak for myself?

That is the part that stayed with me. My episode came with an on-off switch, so I won't claim I know what mania feels like. But plenty of people live in states like that one with no switch at all. Maybe some tiny region of their brain is slightly over-stimulated, chemically or electrically, and bringing it down a bit would change the behaviour. And what do we do with those people? We don't look for the spot. We lock them in a cage, take away all their freedoms, and then act surprised when they come out the same or worse.

Perhaps we are the ones who are really deranged.

Two years later, I walked into another programming session feeling like shit. My gait and balance were bad enough that getting to the clinic was a challenge. My tremor and stiffness made me look like an old decrepit man. The dystonia along my right side was creeping back. And underneath all of that, the anxiety and depression were back too.

The depression had a shape by then. It would start almost every morning, half an hour to an hour after I got up, a churning in my gut, appetite gone, and a feeling that life itself was hopeless. Not just my life. Life. A cruel joke the universe was playing on us all. I would look at other people and wonder what the hell they had to be so happy about.

I had tricks for it. A walk. The gym. Yoga. Burying myself in work until the feeling passed. Sometimes the only thing I wanted to do was go upstairs and cry.

And from the outside, my life was going as well as it had at almost any point in the last decade. I had a girlfriend I had just moved in with. A job that let me work on my own time from anywhere. A book on the way. A company I had helped start. What more could a guy want, right?

I ran through the explanations, the label, the chemistry, the weather, the progression, and none of them answered it. The feeling didn't care how good things looked from the outside.

What fixed it, that day, was a small adjustment to the stimulator: the amplitude turned up by 0.9 milliamps, to the upper threshold of my limits. That is what happened to me; it is not a prescription for anyone else. But the churning stopped, and the hopelessness lifted, and I got to feel like myself again.

Feel like myself again. After the mania pieces, that phrase lands differently. Which self? The one before the current, or the one the current restores? The one who watches the dial, or the one the dial is turning?

I wrote, years later, that a cured tremor means little if the cost is the patient left wandering a strange city with a stranger's impulses, that if we only focus on healing the brain, we risk losing the person inside. That is the whole chapter in two sentences. The tremor is the easy part. The person is the hard part.

There was another cost I hadn't expected: the stigma. Every relationship changed a little, to my parents, to my friends. Not necessarily good or bad. Just different. Altered. An altered state.

It helps to remember the scale of the thing doing the rewiring. Fasano's clinic sees about twenty-five patients in a day. Twenty minutes each. Next visit in six months. Twenty minutes to adjust a dial that can change how a person moves, feels, wants, and is. Twenty minutes, and then the person walks out and lives with whatever the dial did.

So here is where I have landed, for now. I am not the disease, the label never described me, and no dial can. I am not the device either: the current can switch parts of me on and off, but the part that notices, the part that decides what the trade-offs are for, the part that knows the difference between the dial and itself, that part is not a setting. I feel like the same person, same sense of self, same memories, but with a subtle tweak.

The self is the one who answers the question. Who am I doing this for? Me. Not for the room, not for the label, not for the idea of normal. The current can change my tremor, my mood, my impulses. It cannot answer that question for me. Only I can. And as long as I can still answer it, I am still me.

The electricity gave me back more than I had expected: bandwidth. For years after my diagnosis I was trapped in the exhausting cycle of observing myself, chronicling every new tremor, every shift in my symptoms, every inch of my decline. Stabilizing the circuit freed me to stop staring at my own decay and start looking outward. The question at the end of this chapter, who am I doing this for, is the question I carried back into their rooms. Not to ask for a photo op, the way I did in 2018, but to build our own tables.

Chapter 18 — A Seat at the Table

"Nothing about us without us" is the slogan of the disability movement, and the Parkinson's world has adopted it as its own. In October 2026 I sat in the audience at the Michael J. Fox Foundation's annual Parkinson's Disease Therapeutics Conference in New York, two days of the latest science, and counted. A few scattered patients in the crowd. None on the dais. Session after session on biomarkers; almost nothing on the symptoms people actually live with. The one session devoted to patient engagement was thoughtful, well-run, and entirely patient-free. A month later, at the federal Advisory Council meeting in Washington writing Parkinson's recommendations for Congress, a session titled "When Research Reaches People" repeated the feat: zero patients on stage, and across thirty-eight speaking slots all day, I was the only invited panelist living with diagnosed Parkinson's — assigned one question before lunch.

So when they invite you into the room, it is worth asking a plain question: is it a seat at the table, or a photo op? A seat is not defined by the chair. It is defined by what the person in it can change.

Esther Labib-Kiyarash was diagnosed in February 2023, and she had spent her whole career in hospital safety. Her husband is a pharmacy director. When the Parkinson's Foundation announced it was writing a hospital safety guide, about patients not getting their Parkinson's medication on time in hospital, the exact problem she had spent a career solving, she volunteered. She was told to wait. She waited. The guide came out without her.

She went to the working group anyway, in Austin in 2023, a room full of experts from the big university hospitals, and listened to them present a pilot project that had, in their telling, solved the problem. There were no patients in that room. The solution they had arrived at was a computer fix: every hospital should do it on their electronic health record. Esther had worked in hospitals across the country. Every hospital had a different record system, and none of them talked to each other. The paper came out in December 2024, in the Joint Commission's journal, six authors, Michael Okun among them, not a single patient among them.

She spent three years hammering them about it, then stopped and did the thing that actually worked: she taught patients to bring their own medication to the hospital and avoid the hospital altogether. One of them, Beatrice, went in for a hip replacement and was not given her Parkinson's medication on time, so she did what Esther had trained her to do: she hid her own pills under her pillow and took them when she needed them. That is not a workaround. That is a patient doing the hospital's job for it, in secret, because the hospital would not do it in the open. At the last board meeting she attended, the strategic plan had already been finalized before the board saw it; she told the two movement

disorder specialists in the room that they had one job and one job only, to keep patients safe in the hospital, and they were failing. In October 2026 the Parkinson's Foundation emailed to ask her onto a council to roll the model out to smaller hospitals. Three years later, now they want a patient involved. Her line, and it is the truest thing anyone has told me about how patient involvement actually works: if you want anybody to listen to anything you said, it takes about three years.

Esther got that email in October 2026, the same month I sat in that patient-free room in New York. For me, the lesson that presence isn't power was already eight years old. I learned it in Montreal.

Montreal

Montreal. Ziv Gan-Or had invited me to speak to his students and colleagues at McGill for four hours. It went well. Really well. Afterwards there was a lineup of students waiting to talk to me, and I will confess, without much shame, that I floated out of that room.

Float is the right word, because what it inflated was an idea: a global speaking tour. I called it the Great Debates, a seminar series led by a patient, me travelling to great institutions, dazzling young minds with my prowess. I even made a brochure. The topics I listed for it (lumpers versus splitters, defining disease, open science, learning to fail faster) read now like a table of contents for this book. The tour, I should add, never happened. The brochure did.

What happened instead was an email, in April 2019, from Annabel Seyller, the chief operating officer of the Tanenbaum Open Science Institute. Their Leaders Council, a governing board for the open science initiative made up of fifteen very senior people, liked to open its meetings with a lightning talk from a guest. Would I come and give the patient perspective?

I soon learned that Larry Tanenbaum himself would be in the room. One of the richest men in Canada, owner of my childhood team, the Toronto Raptors, who had just won the NBA championship. A small room, fifteen people, and a man deciding how his foundation's wealth would be spent. I walked in thinking I might walk out with a seat on the board, or something like it.

My body had other plans. My autonomic system, the part of Parkinson's that doesn't show up on a poster, revolted almost as soon as I began. I broke out into a sweaty, tremoring mess in front of that distinguished room, and I persevered, if you can call it that, to the end of my ten minutes.

Tanenbaum heard me out. He was polite. Afterwards I shook his hand and, because I am at heart a fan before I am an advocate, I asked him: "He stay?" Meaning Kawhi Leonard. He looked at me with a glint in his eye and said, "He stay."

Kawhi left.

And nothing substantive came of the meeting. No board seat, no role, no next step. A handshake and a story to tell friends.

I had been given the room. I had not been given a say. I would learn that distinction again, at larger tables, with higher stakes. But Montreal is where I learned it first.

We asked politely

In March 2018, Karen Raphael, Sara Riggare, Simon Stott, and I published a short piece in The BMJ. We were three patients and a scientist. Simon was then a postdoc in Roger Barker's lab, already the man behind The Science of Parkinson's blog; he is now Director of Research at Cure Parkinson's. He is near seven feet tall and among the most humble scientists I have ever met: quick to self-deprecate, willing to be challenged, and answering patients with patience and respect even when I don't deserve it. The asks were not radical. Patients should be part of the clinical trial design process, "rather than just being told which hoops to jump through, they should be recognized as partners in research." Incentives should reward scientists for more than high-impact journal placements. Journals should publish replication studies and negative results. Trials should measure what patients care about, beyond the UPDRS and beyond motor function.

The field's senior figures answered, in public, on my site. Roger Barker called the piece "clear, honest and necessary." Peter Schmidt, a senior executive at the Parkinson's Foundation at the time, agreed and added proposals of his own. Patrik Brundin agreed. So did others. Nobody of consequence said we were wrong.

That was 2018. The asks are still open. What grew instead was an industry of engagement: patient panels convened after the protocol is written, listening sessions scheduled after the decisions they might have informed, advisory boards photographed and thanked. Patients get looped in, typically, well after most of the important decisions have been made, and then their presence is cited as evidence that the decisions carry their blessing.

What exclusion costs

Eli Pollard ran the World Parkinson Coalition, and when I interviewed her in 2018 she told me the story she tells to explain why this is not a matter of etiquette. In 2004, a GDNF trial, patients with a pump delivering a growth factor into the brain, was cancelled. The participants, people who had undergone brain surgery for the experiment, learned that it was over from the Wall Street Journal.

Not from the company. From a newspaper.

Pollard had watched the field's engagement evolve since 2004, from treating patients as sources of money and trial slots to formal engagement requirements, and her verdict was that the same mistake gets repeated over and over. She also repeated something a pharmaceutical executive had said to her about why AIDS patients are inside the room in a way Parkinson's patients are not: they are included because the companies are afraid of them. AIDS patients organized as activists. Parkinson's patients were invited to be advocates, a word with the fight politely removed.

The cost of the photo op is not hurt feelings. It is that the people who know what the disease does all day are absent when the questions are chosen, the endpoints are set, and the results are written up, and present when the photograph is taken.

Todd Sherer, who ran the Michael J. Fox Foundation, told me years ago, "[Patients] are the true experts in this disease." The sentence has been quoted ever since. What has not followed it is the restructuring that would make it true in practice, the foundation's own therapeutics conference, eight years after our BMJ piece, still put no patient on the dais. Ray Dorsey put the other end of the experience in one clause: patients in the care system are "processed, much like cattle."

Building our own tables

At some point I stopped waiting for invitations and started building the furniture.

At Toronto Western Hospital, Alfonso Fasano and I formed a Patient Advisory Board inside the movement disorder clinic. Its work is unglamorous and specific: review how the clinic actually runs, its protocols, its instructions, its assumptions, against what is physically possible for someone with advanced Parkinson's. A clinic designed by people who can button their shirts will keep issuing instructions to people who cannot, until someone in the room says so.

The board has family on it now. My mom, Aneta Josefowicz-Stecher, a retired social worker, sits on it as a care partner, and just last week, after four years of her persuading, the clinic finally hired its first social worker. That is not a research breakthrough. It is a person in the clinic whose job is the part of this disease that isn't movement: the forms, the benefits, the family strain, the hundred things no neurologist has time for. It exists because my mom kept asking why it didn't.

I first met Brian Pepin over Zoom, while he was sitting in an airport on his way home to Portland. I opened with a deliberately provocative question: "What is suffering?"

He gave me a thoughtful answer. He talked about his mission in life, and how it had carried him from

electrical engineering to Google to building his own company. I was moved, because it aligned with what I had come to believe myself: that we are here, in the grand sense, to alleviate as much suffering as we can. I told him what that meant for people with Parkinson's: how it's like being slowly tortured to death, only the torturer prolongs the sentence for decades.

That was about it. He had a flight to catch. But the conversation planted something: why and how he should involve patients in what he was building. That notion became the Patient Advisory Board at Rune Labs.

It also became a friendship. Years later, when I woke up robbed in a hotel room in Cartagena, Brian was one of the first people I called, and without hesitation he booked me a flight out of there.

The base StrivePD app was designed and developed by a patient, Aura Oslopas, who sits on the board and now feeds design input to the team as a matter of routine. Patients who use our app also get first access to the data the app generates about them, and they decide who else gets to see their data. That is what the inside of a real seat looks like.

And it has edges, even there. From the board's first days I have pushed for one simple feature: a "Find My Therapist" button, because the therapy that demonstrably helps people with this disease is useless if you cannot find someone who provides it. It has gone nowhere. What I get is continued promises. A real seat, it turns out, is not a veto. It is a place from which you can be refused in person, with reasons, instead of ignored by default, which is better, and is not the same as power.

Martin Taylor, diagnosed at thirty-two, didn't wait for a company to build him one either. He founded the Parkinson's Research Interest Group, patients running an evidence-based forum with ruthless moderation, independent of the big charities, precisely so the agenda would be theirs.

And the newest board, the one I have just begun forming at ModulightBio. Yotam Eldar, the company's co-founder, asked for patient input from the very beginning, before there was a product to react to, because he knows he doesn't understand the patient experience, and needs it in the room while the decisions can still change. Input at the start can cost a company something. Input at the end costs nothing but applause.

And here is what happens when nobody asks at all. In Michigan, Esther was walking to a meeting with her friend Karen and a Harvard neuroscientist, Saranna Fanning, when she and Karen both started to wear off. They both pulled out the same inhaler, Inbrija, a levodopa powder you breathe in when your medication stops working. Esther stopped and made Saranna watch them use it. The cap comes off and has nothing holding it on. The capsule comes out of a blister pack, which is a fine motor task for hands that are shaking. The powder gets over everything, your clothes, your car, and looks, as Esther put it, like you're doing cocaine. Saranna watched and said, oh my god, who

designed this? The drug was developed by Acorda and is now owned by Merz, which bought it in 2024. Esther has raised the design with the company. To change any of it, they told her, they'd have to put it through FDA approval again. The drug itself was approved in 2018. It only reached the UK in June 2025.

Yotam asked for patient input before there was a product to react to. Nobody asked about the inhaler at all, and the device is the evidence. As Esther put it, inhaling a powder that I choke on while trying to hold four components with two hands, one of which is shaking.

The test

Karen Raphael, the professor who co-signed the BMJ piece, gives patients one piece of advice about trials: if there is not a guarantee that you will see the results of the study, walk out.

It generalizes. Before accepting any seat, ask three questions. Was I in the room when the question was chosen, or only when the results are announced? Will I see the results, including the negative ones, in full? And if I say no, does anything stop?

If the answers are no, no, and no, it isn't a seat. It's a photograph, and your face in it will be used as evidence that patients were consulted.

The flagship test

The obvious place to apply that test is the Michael J. Fox Foundation's Patient Council — the formal patient body of the field's flagship funder, in existence since 2009. It is not a sham. Its members are recruited for their experience, meet the foundation's leadership, are encouraged to challenge it, and sometimes shape its communications and programs. Just as important, the Council gives its members something no metric in this book captures well: each other. For many patients, that community is reason enough to stay.

But run the questions. The Council was not created with decision-making authority. Its members advise; the foundation decides. The remit is broad enough that a member can be left to work out for himself where his contribution is supposed to land. The Council's influence rises and falls by year and by issue. And there is no formal ledger of advice given, accepted, rejected, or ignored — no way for a member to point to a decision and say, with proof, *that happened because we said it*.

That is the difference between a seat and a say. Council members can be heard, and sometimes heeded, while still holding no power the institution is obliged to answer to.

What a seat is not

A seat is a beginning, not a settlement. It puts patients in the rooms where decisions are made; it does not pay them for their expertise, train them to use it, or embed them in the institutions permanently enough that the seat survives the person sitting in it.

What that would take is the next chapter's argument.

Chapter 19 — Pay, Train, Embed

I have helped set up six patient advisory boards, two at large pharmaceutical companies, three at biotech startups, one at a major movement disorder clinic. The boards that worked had three things in common, and the ones that decayed into rubber stamps were missing at least one of them.

To put it simply, pay us as experts. Train us as needed. And embed us where the decisions are actually made.

Pay

Let's start with the money, because money is where the politeness ends.

Every institution in this book runs on expertise, and it pays each accordingly. The statistician is paid. The regulatory consultant is paid. The key opinion leader with his name on the protocol is paid, at rates nobody apologizes for. The patient is expected to feel privileged to be included.

So the rule on every board I help build is the one I published in my advisory-board guide: members work as independent contractors, at $150 to $300 an hour, and are treated as any other consultant or key opinion leader would be. Or, as the guide's summary puts it: treat them like what they are, skilled consultants, and pay them as such.

The Roche story in Chapter 6 belongs here, too, not for the fee, but for what came after. I have since watched how rarely patients do that, how often we are so grateful to be asked that we hand over the one thing we have that the institution needs, for free, and call it access. Demanding payment is not greed. It is how you find out whether you were invited as an expert or as decoration.

I can give you my own example, because it makes the point better than the rule does. At Rune Labs I am on retainer, 4,300 Canadian dollars a month, and the board I chair there has real work to show for it: a hackathon that drew over forty engineers worldwide, a study launch, partnership input on deals with BlueRock and Aspen, and a product now downloaded some twenty thousand times, whose original version Aura Oslopas designed from scratch herself. At Toronto Western, the clinic board I formed with Alfonso Fasano, nobody is paid. We are all volunteers. I am proud of what that board has done. I am also telling you plainly: the volunteer board runs on goodwill and spare hours, and the paid one runs like a department. The same company taught me the other half of that lesson.

Rune Labs' first onsite meeting. The company had rented out the Monterey Bay Aquarium for the evening, and there we sat in front of a giant aquarium, eating fish, getting to know each other. I was

with some of Rune's engineers, and I was quietly getting annoyed. The company was around sixty people at the time. I kept doing the math in my head: what must this evening have cost, and how much good could that money have done elsewhere?

Then Brian came over, and I popped. I lectured him, in his own company and at his own dinner, on the sheer waste, and on how much more suffering that money could have alleviated had it been spent elsewhere.

To his credit, he took it calmly. He didn't push back, didn't pull rank, didn't perform being wounded. He just listened.

Later he explained it to me. Evenings like that one do something for a team that no team meeting can: they make people feel they belong to something, and they give them a story to tell. And in the Bay Area, where software engineers are in very high demand, stories like that are recruitment tools. The aquarium isn't just a perk. It's how you get the best people to choose your problem over someone else's.

I have thought about that dinner a lot since. My instinct that night was this book's instinct: follow the money, count the waste, ask what it could have bought instead. Sometimes that instinct is right. But that night it missed something. If you want the best people working on your problem, then at times you need to treat them like the best.

It is the same rule I argue for patients in this chapter, applied to engineers instead. Treat people like what they are, and pay them as such, whether they are engineers you need to woo or patients you need to hear.

Set both beside the flagship. The Michael J. Fox Foundation's Patient Council, the patient body of the biggest funder in Parkinson's research, the model of engagement everyone cites, pays its members nothing. I don't doubt the members' sincerity; some are serious people. But a council you don't pay is a council you never have to listen to, and seventeen years on, the arrangement has produced roughly what it was priced for.

Train

Here is the part where I have to be honest about my own boards: we do not train anybody.

The members are handpicked, by me, mostly. They are professionals: lawyers, engineers, developers, designers, social workers, scientists, people with ten or more years in demanding fields who happen to live with Parkinson's or care for someone who does. They arrive pre-formed. Whatever training

happens is absorption: you sit in enough protocol reviews and data readouts, some of the science rubs off. Nobody designed it. Nobody teaches it.

I know what the self-taught version costs, because I lived it. Mine was the self-taught route of Chapter 1, index cards and cold emails, and it worked, eventually. It is also a ridiculous way to build expertise: it selects for the stubborn, the literate, the ones with the time and chutzpah to bang on every door imaginable, and it leaves everyone else outside.

My friend Jon Stamford has a name for what is missing: a Top Gun academy for patient advocacy. Train patients in the science the way you would train anyone you intended to rely on, how trials are designed, how endpoints are chosen, how to read a results table and spot what it is hiding, and graduate people who can walk into a protocol meeting as peers, not as guests. The design spec is not mysterious. Real expertise, in any field, comes from the same two ingredients: an environment where your judgments get tested against reality, and feedback fast enough to correct them. Patients get neither. We get a diagnosis, a prescription, and a pamphlet.

Until training exists, "patient expert" will keep meaning the same small circle of us, the ones who trained ourselves. That is not a pipeline. It is a bottleneck with good PR.

There is another reason the training can't wait, and it is the one nobody wants to say out loud. There are only a handful of us doing this work, and we're not going to be around forever. I have had Parkinson's for thirteen years. The people who know how to do this work are the same people the disease is taking. If the next generation isn't trained, there won't be one.

Let me be precise about what the expertise is, because the argument depends on it. A trained patient is not a cheaper scientist, and nobody should want us picking molecules, judging molecular biology is not the expertise on offer, and pretending otherwise hands the skeptics their easiest rebuttal. What we know that nobody else in the room knows is which questions are worth a patient's years, which endpoints measure a life rather than a clinic visit, and what a protocol actually asks of the human being expected to endure it. That knowledge is real, it is scarce, and it is exactly the knowledge the system currently gets for free, gets late, or does not get at all.

Embed

Payment makes expertise a transaction. Training makes it real. Embedding is what makes it permanent: putting patients inside the machinery, early enough and routinely enough that removing them would break something.

The mechanics are not glamorous, which is probably why they work. A board starts with a written

proposal that ties the organization's own goals to what the board will do, not "patient engagement," but named projects. The chair meets the chief executive every two weeks, thirty to sixty minutes, with a running log of what was raised and what happened to it. Every member is paired with a counterpart inside the company, a buddy, and they talk monthly, so the relationship is with the institution and not just its leadership. Every quarter, the departments present their projects to the full board for critical input, before the decisions, not after. At Rune Labs, the chief executive at the time, Brian Pepin, backed this structure early, and he deserves a lot of the credit for why it held.

In research, embedding goes further than advice. Patients belong in the design of a study, in its implementation, in the interpretation of its results, and, this is the part that gets skipped, in the governance of its data: who gets to use it, and for what. Sara Riggare taught me that list, and in a decade of sitting in these rooms I have rarely seen all of it honoured. Usually we are consulted on the brochure.

The same principle applies to the 250,000+ neural implants already inside us, whose outcome data Medtronic, Boston Scientific, and Abbott still treat as proprietary. A right to read should be the price of approval: no device trial or commercial rollout unless the patient automatically owns the raw neural and outcome data streamed from their own skull. Call it a right to repair for the brain, or a right to read. Either way, the data is the patient's before it is the company's.

I once tried to spec an alternative way of running a study. TESOBO, tackling each symptom one by one, was a small experiment I proposed in 2022: take one measurable symptom, tremor, put ten to twenty tremor-dominant patients on continuous monitoring for two weeks, measure everything, and publish everything openly, with patients inside the design from the first question. It included one condition I have never improved on: *Also, pay participants, which is self-explanatory, I hope.*

The reason embedding matters is that institutions optimize for what they measure, and what they measure rarely includes us. Alberto Espay has pointed out the ugliest version: surgical centers judged by how many DBS surgeries they perform have an incentive to operate, not to select. A true measure of success, he says, would be fewer surgeries, the right ones, on the right people. You do not fix incentives like that with a patient on a panel once a year. You fix it by having patients inside the room where the metrics are set.

It can scale. In the Netherlands, ParkinsonNet built a national network of specifically trained therapists working to shared standards, and it improved care while saving money. And it can be as local as a clinic. Alfonso Fasano has spent years replicating himself, forty+ fellows trained and sent out, and the Toronto Western board sits inside a clinic built on that premise: that expertise about this disease should be a system, not a personality. The social worker my mother fought to get onto that clinic's staff, in the last chapter, exists because a patient body was embedded deeply enough to ask

why she wasn't there, and to keep asking.

And the agenda does not end at the laboratory door. Some of the most useful things an organized patient community can win have nothing to do with molecules. Certain chemicals, paraquat, the industrial and dry-cleaning solvents TCE and PCE, a list of pesticides, are linked to a higher risk of this disease. We do not know exactly why one exposed person gets sick and another does not, and we may not need to. Nobody fully understood why one smoker got lung cancer and another never did; discouraging smoking still cut the incidence. Prevention does not have to wait for a mechanism. What it needs is a voice with standing to say, early and in the open: discourage the exposures we already suspect, the way we discouraged cigarettes. Not prohibition: pressure. No trial has to read out before that benefit arrives.

Pay, train, embed. That is the whole blueprint, and it fits in one sentence because it was never a knowledge problem. It is a will problem.

It also has a limit, and the limit is geography. Everything in this chapter presumes there is an institution near you with a table to sit at. For most people with this disease, on most of the planet, there is no table. That is where the next chapter goes.

Chapter 20 — How to Feel Better Tomorrow than You Do Today

The last chapter presumed something most patients don't have: an institution, nearby, with a table to sit at. This one starts from the opposite end, not with the system at all, but with the only promise in this book I am willing to make to another patient. It is the sentence I have been closing talks with for years: you can live a little better tomorrow than you can today.

I should be honest about my own standing to say it. I live in Toronto, a short trip from one of the best movement disorder clinics on earth. My neurologist is a world authority who answers my emails. When my medications stopped being enough, I got a machine implanted in my brain that gave me my life back, programmed by people at the top of the field. My recovery, to a disease defined in medical textbooks the world over as degenerative, is the exception, not the rule. Everything that made it possible already exists. None of it is a cure.

What helps today

Start with a trampoline. In Lisbon, a physiotherapist named Josepha Domingues put me through her trampoline jungle gym, bouncing, balance work, movement drilled like play, and an afternoon of it did more for my body, temporarily, than anything the thousands of doctors and scientists I had spent years interviewing had on offer. I wrote at the time that if you could clone an army of her, you would beat almost any drug in development. I have had years to reconsider that sentence. I stand by it.

I had seen the fuller version two years earlier in the Italian Alps, at a centre built entirely around intensive therapy for Parkinson's: patients come for weeks of concentrated, multidisciplinary work, physiotherapy, occupational therapy, speech, exercise, education, delivered by people who treat nothing else, and they go home measurably better at living their actual lives. No molecules were discovered there. No one's disease was cured. People ate better, moved better, fell less, understood their own condition better. It remains the most useful building I have ever walked into as a patient.

That is the model this book keeps circling, so let me say it plainly once: build the network. A global chain of intensive therapy centres, modelled on that one, where the treatment is the patient's actual day, gait, voice, sleep, mood, confidence, and where the advocacy blueprint from the last chapter is built into the walls: patients trained in the science, embedded in the clinic, paid for their expertise, teaching the newly diagnosed what no pamphlet can. We know how to do every part of this. The knowledge is not missing. It is simply not where the money goes, because none of it can be announced as a cure.

I saw the reflex up close in Washington that November, at the federal Advisory Council on Parkinson's. I had just finished asking the council to put federal dollars into multidisciplinary care-and-trial centers when the microphone went to Deborah Brooks, CEO of the Michael J. Fox Foundation. Her immediate pushback centered on cost: *That's expensive — who pays for it?* The foundation she runs has deployed billions of dollars, and commits hundreds of millions every year, into the exact biomarker pipelines and molecular shots on goal I had just critiqued. Nobody in that room asks who pays for it when another nine-figure sum is committed to a surrogate biomarker. The question only appears when the money is asked to go toward care.

And the money *can* be aimed differently: there is a funder proving it. Jonathan Silverstein was diagnosed with Parkinson's and learned he carries a GBA mutation, one of the few subtypes of this disease we can actually define. He was not a dabbler before this happened to him: he had spent his career at OrbiMed, one of the largest healthcare investors in the world. In 2017 he founded the Silverstein Foundation for Parkinson's with GBA, and he runs it the way patients run things when they're allowed to: thirty-nine grants to companies and academic labs, every one of them aimed at his own subtype; four companies the foundation helped co-found have compounds approaching Phase II trials, as of writing. It is the most disciplined money I know of in this field.

Full disclosure, because this book demands it of everyone else too: Jonathan gave me, a fellow patient, the chance to help him run it. The foundation's centre of gravity now is the fellowship program we built together, one of the things in this work I am proudest of. Twenty-six fellows, at seventeen institutions in seven countries, on two-year postdoctoral fellowships with full salary, all working on GBA-PD: how the cell's recycling system fails, why the same mutation fells one carrier and spares another, and what DBS does to carriers over the long term.

The fellowship is also designed so the work doesn't end when the funding does. The fellows present to each other quarterly, one such meeting is happening as I write this, and at the foundation's Industry Insights meetings, the leading companies in this space present their programs to the fellows. When a fellowship ends, the researcher walks into this field's labs and companies already knowing the people, because the community was built around them on purpose.

That is the part worth staring at. Not the generosity: the structure. A patient at the helm. Patients beside him. Money pointed at a defined slice of the disease, and people trained to carry it forward, instead of sprayed at a slogan.

I can't help thinking it, so I'll write it: if we'd had a patient like him, willing to get his hands dirty, at the helm of the Michael J. Fox Foundation, we'd be much further along today than we are.

The second thing that helps is already in patients' hands, and mostly the system ignores it. Every

single day, patients run experiments: a dose timed differently, a walk before breakfast instead of after, a protein-heavy lunch that swallows the afternoon's medication. Diabetes got its revolution when the tools reached the patient: glucose readings at home, pumps, then closed-loop systems that dose on their own readings. Parkinson's is getting the same tools a century later: watches that count tremor and dyskinesia hour by hour, records a patient can actually learn from. A patient who can see their own disease can start steering it. That is not a metaphor. It is most of what "living better tomorrow" is made of.

Where there is no door

Now the part of the world where my slogan sounds like a rumour.

Omotola Thomas was diagnosed in London in 2016, at thirty-five, after years of tremor that neurologists on three continents never connected to Parkinson's, too young, wrong demographic, the same miss that nearly happened to me in Shanghai. She went home to build advocacy in Nigeria, where she is from. The numbers she works against, from her own accounting from an interview I conducted with her back in 2019: roughly eighty neurologists for a country of more than 180 million people. Sinemet, a drug older than I am, priced against incomes under two dollars a day. Stigma that reads the disease as a curse or a spell. And expired medications, past their sell-by date, shipped to Africa as donations. "If it is not okay for people in the West," she asks, "why is it acceptable for Africans?"

Between Toronto and Nigeria there is a middle I have skipped so far: patients in rich countries who live far from experts, for whom the door exists but is hours away.

Hold her situation up against the argument of this entire book and the book changes temperature. The cure trap is, in one sense, a rich world's argument, a fight over how billions get spent. Most of the world's patients are not in that fight. They would trade the whole conversation, every conference, every pipeline chart, every five-year horizon, for a reliable supply of a sixty-year-old drug and one therapist who knows what a festinating gait is. When I say the system should help people live better tomorrow, for most patients that sentence is not philosophy. It is logistics: a drug on a shelf, a clinician in a county, a number that gets answered.

MAID: The last form of control

There is one more thing "better tomorrow" can mean, and in Canada it is written into law.

Everything in this chapter is, underneath, about control, over a body that increasingly does what it

wants. Medical assistance in dying is the final form of it. I want to be precise about my own position, with DBS working and decades hopefully ahead of me: I still expect to reach a point where I want to decide for myself when and where I leave this world. That is not despair talking. It was the same impulse as everything else in this chapter, planning, while planning is still mine to do.

My neurologist, Alfonso Fasano, sits on his hospital's MAID team, for years its only neurologist. I interviewed him about it in 2021, and what stayed with me was not the philosophy. It was the plumbing. Two independent assessors. Criteria, checked. A process built carefully around one thing: a patient's stated wish about their own life. Whatever you think of the wish, notice the engineering. When Canadians decided that a patient's word about dying should be honoured, the system built a door, put two locks on it, and staffed it. When patients say they want to live better, the wish this whole book is about, it builds a pamphlet.

Fasano also told me the trap inside the law, and it is a cruel one. To receive MAID you must have capacity when it happens. So people who want the option held open find themselves choosing earlier than they want to, dying while they still *can* choose, rather than when they *want* to. The safeguard eats the freedom it was guarding. He described patients rushing a decision out of fear of losing the ability to make it, and he did not call that freedom. The freedom to choose becomes the pressure to choose early.

And underneath even that sits a question from my friend Dr. Jennifer Sharma, a movement disorder doctor who has facilitated MAID, and whose first conversation with me, in 2019, was about death. If you decide now for the person you will become, a person this disease may have changed, who may want different things, who supersedes who? I have spent a whole chapter of this book asking who I am after a machine rewired me. I do not have an answer for her version of the question, and I distrust anyone who says they do.

I am not arguing that a chosen death is a better tomorrow. I am arguing that it belongs in the same ledger as everything else in this chapter: the measure of a system is whether a patient's stated wishes about their own life organize anything real. A trampoline that exists. A drug that's in stock. A therapist within reach. A door, at the very end, that opens when you knock. Most patients, most places, get none of these, not because we don't know how, but because we built the apparatus for a different promise, five to ten years away, forever.

Live a little better tomorrow than you can today. It was never a slogan. It's a work order, and almost nobody has been assigned to it.

Chapter 21 — The Cincinnati Cohort

The pace of therapeutic development is bogged down by a system that cannot keep up with my degeneration.

I wrote that line for a talk about how I ended up in Cincinnati. This chapter is the longer version: the place where I stopped only criticizing the machine and got to watch a different one being built, by the man I built it with.

The paper.

At the end of 2018, I read a paper that changed my outlook on life. It was called "Parkinson Diseases in the 2020s and Beyond," note the plural, and its argument was the one this whole book has been circling: that "Parkinson's disease," as a single clinico-pathologic entity, is a convergence that exists in our filing system, not in our biology, and that progress required replacing it with a divergent, systems-biology account: many diseases, many mechanisms, many subtypes, to be told apart by measurement rather than by which symptoms a clinician happens to see first.

One of its authors was Tony Lang. When I told Dr. Lang how much the paper had rearranged my thinking, he told me to seek out his co-author: Alberto Espay, in Cincinnati.

Tony Lang deserves more than a cameo in this story, because Alberto and I both worked on ground he built. At Toronto Western, Lang had assembled the team, lab, clinic, imaging, epidemiology, everything in between, into what is one of the best programs in the world. It is the clinic where my own care is based, and where Fasano and I would later start a patient advisory board. Lang had been saying the umbrella part out loud for years before the papers formalized it: that we were not dealing with a single disease, and that the wins would come five percent of patients at a time, not as a single home run. He co-wrote the papers that said it properly. And then, having helped draw the map, he pointed me at the man building the territory.

In January 2019, Alberto and I started emailing. The correspondence became a book, *Brain Fables*, and the book became a move: I relocated to Cincinnati for nine months to write it with him. The agreement with Cambridge University Press came through in October 2019. I had gone looking for the people rewriting the science. I found the one who was trying to rebuild it, and I went to work beside him.

The clinic.

What I found in Cincinnati was, first of all, energy. I shadowed Alberto in his clinic for a day,

Alberto and his fellows working in concert, meticulously, through more than twenty people with an assortment of different neurological conditions. Diagnosing, adjusting, listening. It was my first real peek behind the curtain of how the assembly we call neurology actually works, and it was eye-opening. It humanized the profession for me. It was also exhausting, and humbling, all at once.

Espay and I worked well together. We never really disagreed. I know a memoir is supposed to run on friction, but there wasn't any: what I remember instead is how humbling it was to watch how much energy one man could have: for his patients, for his fellows, and for the wider community of people with Parkinson's and Alzheimer's that he longed to serve. The clinic day and the research program were the same gesture, in the end. Both said: stop looking at the label. Look at the person, and measure what's actually wrong with them.

The program.

The program that came out of that clinic is the Cincinnati Cohort Biomarker Program, the CCBP. It launched in October 2019 with a $3.8 million gift from the James J. and Joan A. Gardner Family Foundation, and its design is *Brain Fables* turned into a protocol.

It works like this. You enroll people across the neurodegenerative labels, Parkinson's, Parkinson's-like, Alzheimer's, Alzheimer's-like, and healthy controls, and you measure everything: clinical exams, imaging, mobile-health data, blood, DNA, RNA, urine, gut microbes. Then, this is the inversion, you analyze the biology *blind to the diagnosis*. The labels are not allowed in the room while the data is clustered. The thinking is that the biology would sort people into subtypes that the symptom-checklist never could, and that each subtype can then be matched to a drug that might already exist. His colleague Kevin Duque, who runs the machine-learning side, put the program's ambition in one line: "one small subtype at a time."

That is also where the word "cure" finally becomes usable again, in the plural. Not *the* Cure, one ending for everyone carrying the same label, but cures: partial, specific, earned one subtype at a time. The first might reach only a tiny fraction of us. It would still be the first honest one.

My name is on the design paper. I don't say that to decorate myself: I say it because it is the "+ Patient" slide from my talks made literal. I wasn't consulted on the brochure. I was embedded in the work, as a co-author, from the design stage. Chapter 19 argued that this is where patients belong. Cincinnati is where I got to live it.

And the thinking has aged well. In 2019, Espay, Brundin, and Lang had predicted the field's mid-2020s reckoning: a therapy aimed at one biological subtype would succeed in that subtype and fail in undifferentiated "Parkinson's," and the failure would be misread as the idea failing rather than the label. In 2026, the ACTIVATE trial, a drug meant to boost the GCase enzyme, tested in people

with GBA-variant Parkinson's, did almost exactly that, as Chapter 13 described. The reconstruction was right about the disease. The question the CCBP now has to answer is whether it can be right *in time*.

The idea that grew.

One thread from those years deserves its own paragraph, because I watched it grow from an endnote in *Brain Fables* into the argument that might matter most. It started as the loss-of-function thread: the possibility that these diseases are driven less by toxic proteins gaining a function than by proteins *losing* theirs, sucked up into aggregates, depleted, missed. I have come to think the frame was too narrow. The honest version is a dual threshold: too much of these proteins is bad for the brain, and too little is bad too. The disease can push the level out of range in either direction.

In October 2020, the Karolinska Institute held a debate on whether protein aggregation was still a valid therapeutic target. Alberto argued the loss-of-function side, with Kariem Ezzat beside him. The numbers I reported then still stagger me: in Alzheimer's alone, thirty-five clinical trials had tested the gain-of-function idea. None had succeeded. And not a single trial, anywhere, had ever tested loss of function.

The evidence for the other side of the threshold is contested, and the honest version says so. In rats, one group reported that silencing alpha-synuclein in mature nigral neurons — removing the working protein from the very cells Parkinson's takes — triggered rapid inflammation and killed half of them. The same group found the same pattern in a small primate pilot. But no other group has reproduced it: another, using the same approach over twelve months, knocked the protein down by more than seventy percent and found no degeneration at all. The death in the first study was fast and inflamed, which points as much at the viral delivery as at the missing protein. And the field's own evidence for the first threshold is real too: extra copies of the gene cause aggressive disease, and in a toxin model, knocking the protein down partway protected the neurons it would otherwise have killed. Too much, and the protein clumps and the cell chokes. Too little, and the cell starves for a protein it needs to work. The protein has a working range. The disease is what happens outside it.

Four years later, the evidence had kept accumulating, including an analysis suggesting the anti-amyloid antibodies might work by *raising* the very protein they were designed to clear. By 2024 the question was getting hard to avoid: what if patients need more of these proteins, not less? And still, to this day, no one has run the trial that would answer it.

The money.

Here is the part where the Cincinnati story re-enters the world of the rest of this book. A design this heretical could not be funded by the ordinary machinery. The design paper says it in the passive

voice of scientific prose, but the sentence deserves to be heard plainly: the study's exploratory, hypothesis-free design "rendered it unsuitable for funding considerations by agencies giving continued preference for hypothesis-based studies based on the prevailing clinico-pathologic model." Read that again. The agencies could not fund the study *because* it refused to assume the answer. So a philanthropist did.

Philanthropy launches; it does not necessarily sustain. So I became, among other things, the program's travelling fundraiser. In September 2021, at a gala in San Diego hosted by Jenifer Raub's Summit for Stem Cells, I brought Alberto to woo the crowd, and woo he definitely did. Lunch on the waterfront that day: Alberto, Dr. Jennifer Sharma, Jenifer, me. Evening: candles, string lights, a flamenco guitarist, and Alberto in a pink shirt, working the room for a cohort study. It worked, after a fashion: the night raised about fifty thousand dollars. Real money, and a pittance against what a program like this costs to run. That was what sustaining the alternative looked like. A patient and a professor, passing the hat.

Not every door opened. I connected Alberto with George Pavlov at Bayshore, hoping the largest private fortune in Parkinson's might follow the Gardner Foundation's lead. The proposal went to a committee. The money didn't come.

Alberto's read, then and now, is that we were rejected because the CCBP posed a risk to the PPMI model. The committee that reviewed the proposal included Todd Sherer, who had run PPMI at the Fox Foundation for years, and who, in Alberto's account, probably influenced the committee single-handedly. The PPMI model, Alberto says, has not changed in fifteen years: it is still about validating biomarkers, whatever the rebranding. A cohort designed to replace the labels was a threat to a cohort designed to keep them. I can't prove his read. I know the money didn't come.

The ending.

The pandemic ended my Cincinnati chapter before I was done with it. In the spring of 2020, with the world shutting down, I tried to renew my visa so I could stay and continue the work. The application was denied. My role, patient advocate, was not deemed essential by the border authorities.

I spent two weeks in quarantine in a crappy Windsor hotel, and then I went home. At home, my condition worsened.

Not essential. I had spent nine months embedded in the one program I know of that was trying to rebuild the science around the patient, and the system, in its bluntest bureaucratic voice, delivered its verdict on what a patient is for. The program is still running. Alberto is still there, still working the problem, and, when I can arrange it, still working the occasional room. We keep going anyway.

Where it stands.

So: seven years after launch, what has the anti-trap produced? The program's own dashboard, updated in August 2026, gives the honest numbers. **1,090 people enrolled**, against a design that called for 5,000. Of those, 871 are in the Parkinson's and Parkinson's-like group; 138 of them have reached a Year 5 visit. Samples are banked by the hundreds, plasma, DNA, RNA, urine, though spinal fluid, the richest source, has been collected from only twelve people. The publications list runs to twenty-two papers, most of them solid clinical work from the center. What it does not yet contain is the program's central promise: a published biological subtype, matched to a drug.

And the cohort itself carries a caveat the design paper didn't plan on: it is 96.7 percent white, in a program that set out to be representative of its city. The umbrella, it turns out, is not the only thing a study can fail to see past.

I don't offer those numbers as an indictment. I offer them as the chapter's honesty. The CCBP asked the best question in the field, and it is discovering what this book has argued from the first page: the constraint was never the quality of the question. It is money that arrives in galas instead of grants, patients who must volunteer in the thousands and mostly don't, and time, the one currency a degenerative disease spends fastest. The trap doesn't only catch the people chasing cures. It catches the people trying to escape it, too, just more slowly.

Chapter 22 — Fund the Future

When I asked Andrew Singleton, a Parkinson's geneticist who co-leads the Global Parkinson's Genetics Program (GP2), how the field should allocate limited funding to maximize benefit for people with Parkinson's, he did not argue for one allocation over another. He said the field tends to avoid that discussion altogether. That avoidance is where I want to start: we argue about which cure to fund, and rarely about how to choose at all. This final chapter is where I would put the billions.

The disclosure, first.

This book has spent twenty-one chapters asking who pays, who profits, and who gets heard. It would be a poor ending if I now championed companies without telling you where I stand inside them. So: I sit on the Scientific Advisory Board of Neuropep Therapeutics, the company built on Ezzat's work, unpaid, though I hold a small stake in the company: if that bet ever pays off, so do I. I am forming a Patient Advisory Board at ModulightBio, the chapter's fifth bet, under a contract the company's lawyers are finalizing as I write. I chair the Patient Advisory Board at Rune Labs, its third bet, a role Rune pays me a monthly retainer for. I am a co-author of the design paper of the second bet, the CCBP. And the first bet is a blueprint of mine, which is its own kind of interest: I would like to be right. Judge all of them the way this book has judged everyone else: by whether the claim is honest, whether it can be proven wrong, and whether it is aimed at someone's tomorrow.

Bet one: build the centers, and put the fleet inside them.

The first bet combines the two proposals this book has already made separately. From Chapter 20: a global network of intensive therapy centers, modeled on the Italian Parkinson's Therapy Centre, places that give patients the concentrated, multidisciplinary therapy we need. And, from Chapter 19: Jon Stamford's Top Gun academy, training patients to be the compensated experts every board in this book has needed. Build them as one, and then do the obvious, radical part: make every center a site of the fleet.

It answers the cohort's quiet failure, and the reason for it is simple: the CCBP asks its participants for years of visits, blood, and spinal fluid, and offers them almost nothing in return. A center that offers the best two weeks of care in a patient's year will not lack for volunteers, or for their annual return visits, or for their samples. The academy graduates staff each site, recruiting, retaining, governing, the pay-train-embed blueprint with walls around it. Care today. Data for tomorrow. The training that makes both honest. The separation of those three budgets is exactly the fragmentation this book has been attacking for twenty-two chapters.

The centers would also host a job nobody has ever owned: an open-access registry of surgical outcomes, by center and by surgeon, so a patient weighing DBS against focused ultrasound against stem cells could read what actually happened to the people before them instead of guessing. But the work of filling it should not fall on the centers. Medtronic, Abbott, and Boston Scientific already hold the outcome data. Contributing it should be the price of selling the device. Right now there is nowhere to go for that comparison. The centers would be the place, and the registry would be the proof.

Bet two: scale the cohort.

Chapter 21 told you what the Cincinnati Cohort has managed on philanthropy and hat-passing. So here is the second bet, and it is not a company. Fund the CCBP the way PPMI is funded, sustained, serious, institutional money, and turn it from a single-center study into what it needs to be to reach its own goals: a multicenter fleet of phenotype-agnostic cohorts, one protocol, every site measuring the same everything, all of it sharing data openly from the start. Powered, at last, to find the subtypes it was designed to find, and representative in a way one city can never be, because the sites would be where the patients are. Its success condition: an end to the labels we now call PD and AD, replaced by biologies with names of their own.

Bet three: fund the ruler.

The third bet is not a therapy at all. Rune Labs' StrivePD platform measures the disease continuously, in the wild, from the patient's own wrist and phone: some twenty thousand people have downloaded it, about five thousand use it actively. Chapters 11 and 13 argued that we cannot fix what we cannot see. A measurement infrastructure is what seeing costs. The tell that the field is not ready: a few companies, Aspen Neuroscience among them, have used Rune's measures as *secondary* endpoints in trials, never primary ones. Companies do not want to be first with an unverified yardstick; regulators cannot bless a yardstick the field has not agreed on. Fund the future and you fund the unglamorous precondition of every other bet in this chapter: a ruler everyone trusts, starting with patients.

The last two bets are different in kind. They are not infrastructure. They are companies. They belong in this chapter as case studies in how translational science should be governed, and only on those terms: a thesis stated plainly enough to be falsified, patients embedded from the start, and an honest clock.

Bet four: replace what is lost.

As *Brain Fables* was going through the final stages of publishing, in 2020, a piece of work reached us too late to be part of the book. In Stockholm, at the Karolinska Institute, a neurochemist named Kariem Ezzat had been studying what happens to a protein as it turns from soluble to solid: from

dissolved and working, to clumped and useless. His experiments suggested something the field had stopped saying: the catastrophe may not be the clumps. It may be what the clumps cost. A protein forced out of solution by contact with an abnormal surface, a virus, a nanoparticle, any of the triggers we cannot see under a microscope, loses its normal function. The brain is not only being poisoned. It is being *depleted* of the working protein.

We put it in the book as a note added at press time. It closed: "Both of us are brimming with anticipation about its translational potential, whose feasibility will be thoroughly assessed in the months to come."

Six years on, the feasibility is still being assessed.

You met Kariem Ezzat in the last chapter, arguing the loss-of-function side of a Karolinska debate in 2020, next to Alberto. Neuropep is his attempt to turn that argument into a therapy, and its thesis takes the press-time note one specific step further: among the proteins the brain is losing are its neuropeptides, the small signaling molecules that keep synapses working. Protect them, and replace them. That is the whole platform, in the company's own two words: *protect* and *replace*.

Protect: an oral drug, built on sacubitril, a medicine already approved for heart failure, whose job is to block neprilysin, one of the enzymes that breaks neuropeptides down. It breaks down Aβ42 too, the peptide dementia depletes, so the same drug raises the protein in the blood. Slow the shredding, and the blood keeps more of what the disease takes away. The drug barely crosses into the brain, so whether the brain does too is what the trial has to show. The most suggestive evidence is not Neuropep's, and the distinction matters. In a retrospective study of 22,626 propensity-matched patients with heart failure, those receiving sacubitril/valsartan had roughly half the rate of diagnosed Alzheimer's disease over three years as those receiving other standard heart-failure drugs (hazard ratio 0.48). It is observational evidence in heart-failure patients, not a Parkinson's trial, and not proof. That is precisely why it will stand or fall in a proper trial. Replace: engineered copies of the peptides themselves, built not to aggregate.

Now the tension, because it would find us anyway: Neuropep's own website uses the word "curative." In a book called *The Cure Trap*, that deserves elaboration, not a shrug. Here is the distinction I would defend. The trap was never a word; it was a transaction, hope sold to donors by people who would never have to answer for the deadline. This bet makes the opposite offer. The thesis is stated plainly enough to be falsified. The first trial rides on an approved drug's safety record, so it can be run soon, and cheaply, and its answer will be an answer — to the question it actually asks, which is whether raising the brain's depleted peptides helps. It will not answer the loss-of-function question about alpha-synuclein itself. That test, giving patients more soluble alpha-synuclein, has still never been run. And the honest limit, which is why the bet is in this chapter

at all: the trial has not started, because Neuropep still has to raise the money to run it. A falsifiable test of an idea nobody has tested sits on the shelf for want of funding, in a field that always finds money for the next promise. Kariem once asked me what Michael J. Fox would say about the loss-of-function hypothesis, and about Neuropep's trials. I still don't know. I know the question has never been put to the flagship by anyone with the power to fund the answer.

Bet five: tune with light.

In September 2026 I spent an afternoon in Boston with Dr. Yotam Eldar and came away thinking I had seen what comes after the blunt instrument, deep brain stimulation, the implanted current that has run my movement for five years. His company, ModulightBio, works on optogenetic neuromodulation: put a light-sensitive protein into a specific set of neurons, and you can switch those neurons with light instead of current, in principle, a less invasive, more precise, more targeted version of DBS.

In the 1990s, Peter Hegemann was studying how a single-celled alga swims toward light. Nobody funded that work to cure anything; it cured nothing for decades; it simply accumulated, paper by paper, into the discovery of channelrhodopsin, the light-switch protein. On October 5, 2026, Hegemann, Georg Nagel, and Karl Deisseroth received the Nobel Prize for it. Yotam raised the prize himself when we spoke, two weeks later, and he raised it for the right reason: the distance between pond algae and a therapy is measured in decades, and the honest response to that distance is not to shorten the promise. It is to fund the distance.

So here is ModulightBio's honesty, plainly, because the chapter's standard demands it: the company is preclinical, and still deciding on its first target; the Parkinson's program rests on animal data. Nothing in this bet can help a patient today, and Yotam says so. Ask him when patients might get it and he gives the field's usual answer, five to ten years, if all goes well. Except he gives the same answer to patients as to investors. And he is building the part I care about now: he has asked for a Patient Advisory Board at the earliest stage, because he knows he does not understand the patient experience and does not intend to design around that ignorance. And if a real trial ever fails, his stated aim is to run it so that the failure teaches the community the most it possibly can. That is what funding the future looks like from inside a company that has not yet earned a dollar of revenue: the clock is the disease's, not the pitch deck's.

The standard.

Lay the five beside the flagship model and the difference is not the vocabulary, everyone reaches for the same words, eventually. It is the structure. Money matched to the disease's clock instead of the grant cycle's. A portfolio of distinct bets instead of a single jackpot on a single protein. Patients

embedded and paid, not photographed. Measurement treated as infrastructure. Yotam's test, offered when he read an early chapter of this book, is the one I would apply to all of it, his own company included: organizations that don't change or evolve with time and data are basically a religion.

Chapter 20 showed what it looks like when a patient runs money with discipline, Jonathan Silverstein's foundation, aimed at one subtype, fellowing the scientists who will outlast us all. Chapter 21 showed what it costs when the design is right and the funding machinery says no; the second bet is simply the bill for saying yes. None of the bets in this chapter promises forever. Each can be checked, soon, against a patient's actual tomorrow, and each can be abandoned in public if it fails the check. That is all "fund the future" means. It is the opposite of a trap, because nothing here needs you to believe.

There is one more ruler to fix, and it is a label. The field calls a therapy disease modifying when it slows the biology underneath. By that definition, neither levodopa nor DBS qualifies, and those are the two therapies that did the most for how long patients live and how well they live it. Before levodopa, Parkinson's mortality ran nearly three times the general population; after it arrived, study after study reported mortality improved, even if it never fully normalized. DBS restores function by retuning the circuit, and people live a long time after it, though no clean comparison has shown it extends life against matched patients who did not get it, and the disease keeps progressing underneath it. I am not claiming DBS slows the biology. I am claiming the label is the wrong ruler. If the therapies that help patients most are both filed under symptomatic, then disease modifying is measuring something other than what patients need. Fund by lives, not labels.

The missing infrastructure.

These bets are not the whole story. There are problems in this book I could state but not solve, and no startup in this chapter can solve them, because they are not startup problems. They are the missing infrastructure, the things that have to change before any bet in this chapter can do its full work.

The funding clock. Matching money to the disease's timeline is the aspiration. The mechanism is governance: a hypothesis that fails trial after trial should face a sunset clause, an automatic reallocation of the money to orthogonal hypotheses, and adversarial red-teaming before the next round. That is the one reform this chapter asks of the institutions that failed. Every other bet I proposed builds something new; this one asks the existing giants, MJFF and ASAP, to change their own rules. Private foundations do not answer to Congress. They can change their rules tomorrow. Nobody has demanded it of them. Until someone does, the clock has no fix.

Universities reward publishing and grants, not patients helped. Nothing in this chapter changes how academia keeps score.

The funder for un-ownable trials is still unnamed. Public money is the source, but no institution exists to deploy it. The centers are where those trials would finally get run, funded by the redirected money, but the funder does not exist yet.

Patients give their bodies to research for free, the spinal taps, the months of pain, no follow-up. I proposed paying participants, in TESOBO, and no trial has adopted it. The worries are real: money can coerce consent. But paying for time and burden is not paying for risk, and the alternative is asking the poorest patients to donate their bodies for free while everyone else in the trial gets paid. The proposal exists. The practice does not.

There is no method for weighing life-altering therapies against each other. The DBS decision has no decision science. The centers would build the registry that makes the decision possible, but the registry does not exist yet.

Companies own the data your devices collect about your own brain. Chapter 19 demands a right to read it. No regulator has granted it.

Write to me at tmrwedition.com/ps. I'll read all of it.

As I said at the front of this book, some problems are stated here, not solved. If you can see further than I did on any of these, or if you think one of the solutions I did propose is wrong, I want to hear it.

Epilogue — Tomorrow

A note to the newly diagnosed

Learn to live with it.

There is no cure for life, not for Parkinson's, not for anything. This disease will be part of you now, for the rest of your life. I stopped hiding from it. I stopped performing wellness for the people around me. I stopped putting my life on hold until I was fixed, because fixed isn't coming.

I embraced it. Not because it's good, it isn't, but because it's mine, and every ounce of energy I spent fighting its existence was stolen from the life I still had. The people who do best with this disease aren't the ones with the best doctor or the best drug. They're the ones who stopped negotiating with reality the earliest.

You still have a life. It won't be the one you planned. Some days it will be smaller than you want. Make those days count anyway. And on the good days, there will be good days, don't waste a single one waiting for a cure that will never come.

Tomorrow. That's the whole standard. Live a little better tomorrow than you do today, and you've beaten everything this book is about.

A last word to patients

Stop lending your bodies to trials that use you. Demand trials that serve you.

The power is in our hands, but only if we take collective action. If we never exercise that power, it will never be useful for us, and these companies will keep treating us as cattle they can herd in whatever direction they please.

Acknowledgements

A book like this is not written alone, whatever the cover says.

Alberto Espay has been arguing with me, productively, for years. We wrote *Brain Fables* together, and I moved to Cincinnati for nine months to work closely with him. The Cincinnati Cohort is his work, and Chapter 21 is my attempt to say what it showed me. When the foundation that funds him promoted a staging system built on its own biomarker, Alberto published the refutation, and when Chapter 4 of this book was drafted, he read it and sent encouragement. That is what a scientist is supposed to do.

Alfonso Fasano co-wrote *Reprogramming the Brain* with me. He ran the trial in which my adaptive DBS was switched on, and we built the Toronto Western Patient Advisory Board together, patients inside the clinic, reviewing protocols, saying what works and what is physically impossible for someone with advanced symptoms. He has also been my fairness check for years. When my argument gets too pleased with itself, Alfonso is usually the person whose objection I have to answer. This book is better for every one of those objections.

Gerold Riempp was as instrumental as anyone in shaping how I think about this disease. I spent four months in southern Germany learning from him, and he taught me that Parkinson's is a systems failure, not a single broken switch: mitochondrial, lysosomal, inflammatory, all of it at once in the same brain. The argument of this book runs on that lesson. Gerold is a professor of information systems who lives with Parkinson's himself, and he approached the biology of his own disease the way a systems architect maps a failing network. When I asked him in 2018 whether I should urge patients not to join monotherapy trials, he counselled patience and told me to focus on proving the better design instead. Eight years later, the evidence did the proving.

Tony Lang built the Toronto Western Movement Disorder Clinic into one of the best programs in the world, and it is where my care is based. When a paper, *"Parkinson Diseases in the 2020s and Beyond,"* note the plural, rearranged how I thought about this disease, I brought it to its author, Tony, who graciously pointed me to its co-author, Alberto Espay. *Brain Fables* came out of that introduction. Chapter 21 tells the story in full; it is recorded here too, because a page of thanks that left him off it would be false accounting.

Patrik Brundin gave me my start. He invited me to co-author the paper that proposed dividing Parkinson's pathogenesis into triggers, facilitators, and aggravators, and that invitation, before I had any standing in the field, was my way into the scientific conversation. He is now at Roche, leading their movement disorders work.

Ziv Gan-Or invited me to McGill to speak to his students and colleagues for four hours. I have called that invitation, in some ways, the launching point of my career in advocacy. He was right that a patient should be given the room for that long. Special thanks.

Jeanne Loring helped launch the ride this book is the record of. Hearing her talk about the potential she saw in Shinya Yamanaka's Nobel discovery, induced pluripotent stem cells, to help people with Parkinson's was truly inspiring, and I have never forgotten it. It showed me what basic science can do when it is aimed at people's lives: a discovery about how cells work, turned toward a disease that destroys them. Her words of encouragement, when they arrived, were welcome. Her example, years earlier, was more than welcome. This book is hard on how science is funded and aimed. It has never been against the science itself, and Jeanne is a large part of why.

Andres Bratt-Leal stood beside Jeanne in that early work, and beside me in the early days of this ride. Everything they did to get it started, I remember. His encouragement now means as much as his help did then.

Steffany Bennett runs her lab the way I wish every lab were run. I toured her neurolipidomics lab in Ottawa, and what I found was patient-centered and empathetic, science done exactly the way science should be done. If every lab were built like this one, I told a friend, I would have no reason to write this book. That is both the highest compliment I can give and the whole argument of these pages: the science is not the problem. How it is built, and who it is built for, is.

Samuel Burke has been asking awkward questions about the evidence ever since we met in 2019, and has become one of my closest collaborators, stress-testing every hard idea I have in the field. He walked me through the neuropathology paper at the heart of Chapter 11, a paper he co-authored, and taught me to ask whether the lights had been counted right. He read early chapters and told me plainly where a reader might get lost.

Rebecca Miller read this manuscript the way I hoped someone would: closely, and arguing back. Her challenge to an early draft of Chapter 4, that it couldn't just be two people in a room deciding where the money goes, produced the passage describing the Foundation's scientific machinery. Later in the process she read the whole book and came back with sixteen points. Many are in the text now, including the fuller account of the PASADENA and PADOVA trials in Chapter 6, and a reordering of Chapter 4 that puts the description before the critique. She was right. It is a stronger chapter for it.

Kariem Ezzat read Chapters 4 and 7 together and saw that they were the same story told twice: the thought leaders define what counts as leading science, and the money follows. The bridge sentence in Chapter 7, the thought leaders defined it, the checkbook followed, is there because he said it first.

Yotam Eldar read Chapter 4 early, pushed back where he thought I was being unfair, and sent

encouragement when it counted. An afternoon in his Boston office became the fifth bet of Chapter 22. We are now building a Patient Advisory Board together at ModulightBio.

Brian Pepin has been arguing about this field with me for years. We co-wrote a piece on why we fail to treat neurodegenerative diseases, and he helped me think through the mechanics of embedding patients on boards that Chapter 19 describes. He was also one of the two readers who talked me off a back-cover line that didn't work. They were right, and the cover is better for it.

Ro'ee Gilron helped build the adaptive DBS technology that gave me my life back, which is not the usual starting point for a book's most searching critic. He read most of the manuscript and sent the critique I have sat with longest: that the chapters jumped between memoir, science, and argument without connective tissue; that a few passages read like keeping score; and that pieces I had written chapters apart, the damage already done by diagnosis, slowing versus reversing, the problem of finding the people who will actually get sick in time to prevent it, needed to be tied together. They are now, in Chapter 13. He also told me, in the last paragraph of his note: "You don't need to prove that the entire establishment made the wrong bet for your experience to matter." It's the kindest version of the hardest thing anyone has said about this book.

Esther Labib-Kiyarash was one of the first people to read this manuscript, and the first to make it better: a note from her cut a weak, bolted-on ending from Chapter 4, and the chapter now ends where she said it should. Her encouragement, when it came, was specific, the only kind worth having. She also sent me, in a string of voice notes, the stories that sharpened Chapter 18: three years of being told to wait while the Parkinson's Foundation wrote a hospital safety guide without her, a working group with no patients in the room, and a pilot project that solved the problem on paper while the ward stayed the same. And, in Michigan, two patients struggling with an inhaler no patient had been asked about, in front of a Harvard neuroscientist who asked who had designed it.

Sree Sripathy is a fellow patient advocate whose judgment I trust. She read the manuscript and told me two things: that it resonated, and that it needed to be tighter, with more lines a reader could carry away. She was right on both counts, and a full revision pass followed from that note.

Rich Sussman read the whole manuscript and sent his responses in two halves, agreeing where he agreed, pushing where he didn't. He and his wife, Pola, advocate in this world as a patient-and-care-partner pair, and his challenges came from inside that experience, including a fair question about how many patients could justify being paid as experts. One of his suggestions is in the text: that an organized patient community can fight to discourage the chemical exposures already linked to this disease, the way smoking was discouraged, prevention that doesn't have to wait for a mechanism. He was right, and Chapter 19 is stronger for it.

Jon Stamford is a fellow patient advocate who has been thinking about how patients get trained for longer than almost anyone. The Top Gun academy for patient advocacy that Chapter 19 argues for was his idea before it was my chapter. He also read Chapter 7 and told me, as a friend, where its tone was working against it. Both gifts are in the book. We have since talked about the book, and he told me plainly what he thinks: that it is too long, and that parts of it read too much like AI. I disagree about the length. I accept his criticism all the same.

Heidi McBride taught me how to tell a good biologist from a great one. She can close her eyes and picture the cell she is working on, not a diagram of it, the thing itself. Some biologists can do that. Most cannot. I have judged almost every biologist I have met since by whether they can.

Jan Stoehr runs Parkinson's discovery at AbbVie, and he read this book the way I hoped someone inside the industry would: at full strength, arguing back. His was the strongest statement I have seen of the case that the system's check-ins and disciplines serve a purpose, and his questions made several of mine answer harder versions of themselves. We disagree about a great deal, starting with synuclein. A book that argues the field should welcome dissent should be able to thank its own dissenters, and I do.

Tilo Kunath is the rare scientist who disagrees with you properly — in full, and with evidence. We toured Edinburgh together, he and his son and I, and hiked Arthur's Seat, and he asked me a ton of interesting questions about what living with Parkinson's is actually like. We have not always seen eye to eye, on synuclein mainly, and I still deeply respect him. After he read the manuscript, he spent an hour walking me through a slideshow he had made, arguing, with the papers to back it, that there is no evidence loss of α-synuclein function causes Parkinson's, and that the protein is protective before it becomes pathogenic. I owe him an apology: I could not sit on this book any longer waiting for his written comments, so it goes out with his challenge unanswered.

Yoann Joyeux is a fellow patient advocate who read the manuscript from rural France, far from experts himself. He pushed me on three points: that pay, train, embed still leaves patients advising other people's research, and the next step is patients leading it; that the access story has a missing middle between Toronto and Nigeria; and that the interventions nobody owns are the ones nobody tests.

Lorraine Kalia, editor in chief of the Journal of Parkinson's Disease, made me rethink how this book treats its cast. Her point was not about caution, but about readers: a reader outside the field should be told who the people in this book are — their place in the field, their personality — not only their names, and some of them may not need naming at all if the description itself does the work. That changed how I think about characterization in these pages, and I am grateful for it.

Simon Stott is Cure Parkinson's director of research, and we co-authored the 2018 BMJ piece calling for the field to reform itself. He read this manuscript all the way through and gave me the bluntest verdict I have received: three parts not yet connected, and a warning I am taking seriously, that making an example of individuals risks burning bridges the cause needs. Hate the game, not the player. He is right about the distinction, and I am grateful for the bluntness. His "three disconnected books" verdict is also what sent me back to map every problem in this book to the solution meant to answer it — a map that became 'The missing infrastructure' at the close of Chapter 22.

Mateusz Zurowski is my neuropsychiatrist, and he read this manuscript the way a clinician reads: for what it claims, not for what it feels. He caught an argument I had left incomplete in Chapter 8, that the system is frozen not only because funders control the purse strings but because the same loop manages what gets published, who speaks, and who gets the chair. The chapter is more honest for it, and I am grateful.

Michael Unea has known me since childhood. When the cover was stuck, he suggested a mousetrap, the pill as bait. It says in one image what I needed a subtitle to explain.

My uncle, Felek Jachimowicz, read the manuscript the way he does everything, completely. His questions were diligent enough that several of them changed the text, Chapter 4 included. He is also quoted in these pages: the closing line of Chapter 2 is his, and it is better than anything I was going to write there.

My aunt Vera read the manuscript as the reader I most need and most fear: someone who owes the book nothing and will simply stop reading. Her verdict, too much information, the structure too dense, was the first warning that the book was asking too much of its readers. Three other readers eventually said versions of the same thing. She said it first.

My mother is a retired social worker who sits on the Toronto Western Patient Advisory Board: her pushing is why that clinic hired its first social worker. As a reader she corrected my own diagnosis story in Chapter 1, and told me in the margins where the manuscript had grown too dense to follow. Every lay reader this book finds, it finds partly because she marked where she stumbled.

My father asked the questions lay readers exist to ask. Why do we measure a disease like this in five-year intervals? And the harder one: who is this book for? The Note to the Reader exists because he made me answer the second.

To everyone else who read drafts, sent papers, argued, and told me when I was wrong: thank you. The errors that remain are mine.

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Each note is keyed to the passage it supports: the page, and a short phrase from the passage itself. Notes are numbered sequentially in order of appearance.

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