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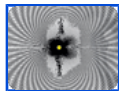
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## A Shock to the System

To slow the progress of Parkinson's disease, doctors planted electrodes deep in my brain. Then they turned on the juice.

By Steven Gulie

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Steven Gulie narrates this montage of images and video.

I'm lying in an operating room at the Stanford University hospital, head shaved, waiting for my brain surgery to begin. Sure, I feel anxious, but mostly I feel crowded. There are 10 people milling about, tinkering with instruments and examining me. It's an impressive crew, including a neurosurgeon and his fellow, a neurologist and her fellow, an anesthesiologist, an experimental physicist, and a graduate student in electrical engineering. That's right, a physicist and an electrical engineer. Directly behind me, out of my sight, is the star of the show, chief neurosurgeon Jaimie Henderson: 44 years old, tall, erudite, and handsome. On my right, flexing my hands, is neurologist Helen Bronte-Stewart: brisk, smart, and beautiful. In fact, nearly everyone is not only brilliant but also pretty enough to play themselves in the movie version of this story. I call them Team Hubris.

Today I'm an honorary member. I'll be kept awake for the entire procedure. During the surgery I will talk and move my limbs on command, which helps Team Hubris know which part of my brain is being poked.

Unfortunately, this also means I'm conscious when Henderson produces what looks like a hand drill and uses it to burr two dime-sized holes into the top of my skull. It doesn't hurt, but it's loud.

Team Hubris is installing a deep brain stimulator, essentially a neurological pacemaker, in my head. This involves threading two sets of stiff wires in through my scalp, through my cerebrum — most of my brain — and into my subthalamic nucleus, a target the size of a lima bean, located near the brain stem. Each wire is a little thinner than a small, unfolded paper clip, with four electrodes at one end. The electrodes will eventually deliver small shocks to my STN. How did I get into this mess? Well, I have Parkinson's disease. If the surgery works, these wires will continually stimulate my brain in an attempt to relieve my symptoms.

The first half of the operation goes smoothly. Through amplifiers connected to the probes, the team can listen to my neurons fire as the wires move through my cortex. This helps pinpoint the location of the probes. When I move a limb, for example, my subthalamic nucleus ignites, resulting in a loud burst of static. The doctors and the physicist practically sing along: "That's driving it!" "Yes!" "Listen to that!" "Dorsiflexion!" "Perfect!" The fellows' eyes are shining. Everyone looks happy and expectant — proud. Following instructions from the neurologist, I tap my fingers, open and close my mouth, stick out my tongue. She is pleased.

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After positioning the first electrode, which takes about three hours, we stop for 10 minutes to prep for the second electrode. I listen to my iPod; several doctors step out to stretch. For some reason, when we're ready to start again, the neurologist, Bronte-Stewart, isn't there. They page her. They wait. They page her again. (She later says she never got the first page.) Eventually, they proceed without her. The neurology fellow steps in, flexing my hands and asking me to stick out my tongue. She doesn't seem too happy.

She's not the only one. Team Hubris is struggling with the second electrode. "That sounds like it, but it's dorsal, too dorsal." "I don't like this electrode." "I don't think it's the electrode." "I think maybe it's a software problem." "Try another cable." "Another audio cable?" "Well ... yes."

Bronte-Stewart returns at last. She relieves the fellow and begins flapping my wrist and flexing my legs. She seems upset. Meanwhile, the physicist and the engineer continue working on the errant electrode. This is not good.

The tremors started in 1999. I remember pouring a glass of wine and my hand starting to shake. "What's that?" my wife at the time asked. "Parkinson's," I joked. We laughed. I was only 43. It seemed funny.

The shaking went away, but over the next few weeks I started using the computer mouse and eating with my left hand. I didn't know it, but the Parkinson's was affecting the fine motor control on my right side. It was subtle, but enough to make me more comfortable as a southpaw. "That's odd,"

I thought. “When did I become left-handed?”

Then I quit surfing. As a Santa Cruz, California, local, I had gone out on the water at Sewer Peak or Steamer Lane almost every day for years. Suddenly I wasn't catching any waves. I just couldn't get the nose of my board down, couldn't coordinate the movements to shift my weight forward and transfer the swell's momentum to my board. “I'm getting old,” I thought. “Old and fat. And weak.”

But I was getting old too fast. I felt like I was 70. Finally, in 2000, I went to the doctor and got the official diagnosis: Parkinson's disease. It affects about one person in 100, usually people in their seventies. I was in my forties. That made me more like one in 4,000. That's like winning the lottery. Whoops, wrong lottery.

Parkinson's causes brain cells in the substantia nigra (Latin for “black stuff”) to die off. This area is where the neurotransmitter dopamine gets manufactured, and without dopamine, the brain's circuits start misbehaving. When the substantia nigra is 50 to 80 percent gone, you begin to experience Parkinson's symptoms: usually tremors but also constipation, stiffness, and depression. You slowly lose smooth motion of all kinds, as well as the ability to feel pleasure. It's a darkness that covers you.

Doctors can't give you replacement dopamine to fix the problem, because dopamine can't cross the blood-brain barrier — the fine mesh that keeps coarse intruders like bacteria out of the brain. Instead they give you levodopa (L-dopa), a dopamine precursor with molecules small enough to slip through the barrier. It's like flooding an assembly line with partly manufactured goods; if one of the workers is in the mood to make a little dopamine, it's easy to finish the product. But many of the workers on this particular assembly line are already dead, and the rest aren't feeling so good. Consequently, production is spotty. And there are side effects. Most of the uncontrolled movements we associate with Parkinson's aren't actually symptoms of the disease; they're caused by L-dopa.

As time goes on and you need more L-dopa to produce any dopamine at all, the side effects become worse. It gets so you can't walk, your movements are so out of control. But it's still better than the alternative: no dopamine, leading to paralysis, the inability to swallow, and death.

Now there's another alternative: a personal brain implant. Doctors can use scans to detect aberrant electrical activity in the brain; they can even localize it in three dimensions through computed tomography (CT scanning). Using this information, they can place electric stimulators directly on a trouble spot. In the case of Parkinson's, the stimulators zap either the globus pallidus interna or the subthalamic nucleus, depending on the type of symptoms you have. The shocks seem to let these parts of the brain function normally despite the lack of dopamine. Over the last decade, the procedure has been performed on more than 20,000 Parkinson's patients.

Of course, deep brain stimulation won't be limited to Parkinson's for long. Many disorders involve abnormal neural activity. Using drugs to combat these glitches is like carpet bombing. It's better to zap the area in a surgical strike — it's more effective, and there's far less collateral damage. Researchers are now experimenting with brain stimulators for epilepsy, obsessive-compulsive disorder, Tourette's syndrome, and depression. Animal studies are under way for it to treat eating disorders. It's a whole new wave of personal digital technology.

Still, when it's you, the idea of having someone saw open your skull and insert wires into your brain doesn't seem like a very good idea. In fact, it seems like a really bad idea. But the Stanford team is one of the most experienced in the world. They are fairly confident that a deep brain stimulator will greatly reduce my Parkinson's symptoms; that it will turn the clock back a year, two years, even five; that I will need to take less L-dopa, have fewer side effects, and live a much more normal life.

By my first meeting with Team Hubris, my life hadn't been normal for a while: I was already stooped and shuffling, dropping things, complaining about my infrequent bowel movements. I couldn't ride a bike. In fact, I had trouble tying my shoes. I could barely type. And the side effects of L-dopa were already showing: flailing motions, weird posturing. Eventually I was forced to take disability leave from my job as a technical writer at Apple. I felt as though I was slowly fading out of other people's lives, out of life itself. Wires in the brain? Sign me up.

**Jaimie Henderson** was tinkering with the brains of Parkinson's patients back when it wasn't fashionable — in the early '90s, when instead of stimulating the brain, doctors would destroy the troublesome parts of it altogether. This was the type of operation Michael J. Fox had in 1998, when doctors surgically eradicated a section of his thalamus. It was effective, but crude. Call it brain surgery 1.0.

In 1995, doctors at Mt. Sinai Medical Center in New York<sup>1</sup> conducted the first US surgery to put stimulators directly into the subthalamic nucleus. Henderson started performing the procedure experimentally in 1999, and in 2002 the FDA approved the use of brain stimulators for Parkinson's. Good health care plans — like the one offered by my employer, Apple — cover the procedure. The cost for mine: about \$250,000.

The heart of the device is a small computer that gets implanted under the collarbone. Electricity flows from this device — the stimulator — through wires running under the skin and the scalp, through the electrodes into the brain, and returns to the computer through the body to close the circuit. The power is always on, so the stimulation is continual. The apparatus is battery-operated, and the battery is not rechargeable. They have to do minor surgery to swap it out every three to five years.

The system can be fine-tuned after the operation by activating various electrodes, shifting the affected area by a millimeter or two. The doctors can also tweak the frequency and amplitude of the electrical stimulation, modify the pulse width, and make other adjustments to the software through a remote control. Wireless? Software? Now that's brain surgery 2.0.

I asked Henderson about features still on the whiteboard: What will be in rev 2.2 or 2.5? He thinks the next release of the stimulator will sense chaotic activity in the brain and turn itself on only when needed. That's on a par with current heart pacemakers, which no longer mindlessly zap you with a steady pulse but actually look for a problem to fix. The next-gen device will also probably be transdermally rechargeable, so you won't need surgery to get new batteries.

It's tempting to wait. But as with any tech product, there will always be the promised next release full of new features. Besides, as Henderson stresses, the current model is a “stable release.” Right. I've got enough problems without having to debug my brain implant.

There will likely be side effects. I may experience speech problems or difficulty finding words. The doctors will try to minimize that by placing the electrodes just right, but things may never be exactly the same. This leaves me with a lingering question: Will I still be me with a brain implant? Well, it depends on how you define “me,” doesn't it? In the sense that “me” is a person weighed down with Parkinson's and almost unable to type or tie my shoes, no. I won't be me anymore.

The surgery normally goes like this: You get one side of your head wired — this takes between three and four hours. Then you wait a week and they do the other side. Wait a week more and get the pacemaker inserted. Wait till the swelling goes down — maybe another couple of weeks — and get it programmed.

But I'm young and strong, and Team Hubris has a hard time coordinating all these surgeries. So they decide to wire both sides of my head in one session, over roughly six hours, to simplify things. The day before the operation, I have screws inserted in my skull. Yeah, screws.

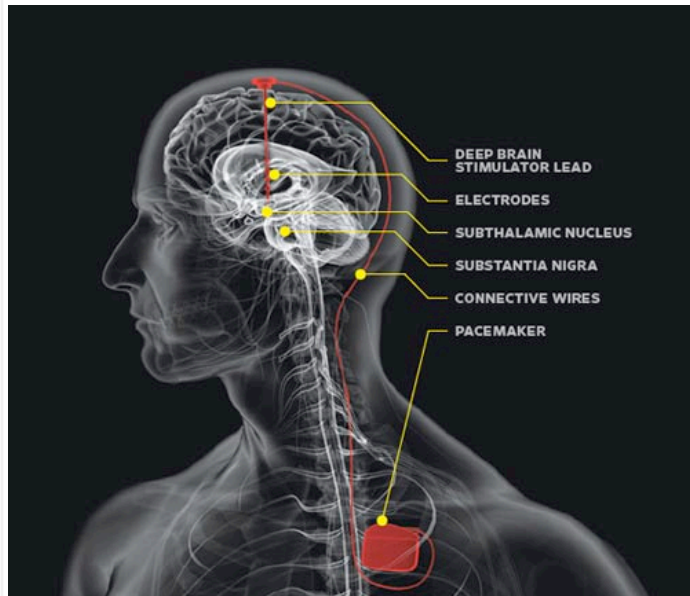
In traditional brain surgery, your head is bolted into a rigid metal frame while your brain is scanned to provide a 3-D model to work from. This model helps doctors plan a pathway to a precise spot in the brain, avoiding major vessels and arteries (nick one of these and it's game over). If your head moves, it no longer corresponds to the model on the screen. This approach is uncomfortable, and it puts the surgeons under serious time pressure.

The screws are an innovation pioneered by Henderson. They allow surgeons to work without a frame for your head. The screws are driven right into the bone using a cordless screwdriver with a Phillips-head bit. It hurts, but not as much as you might expect. When you get scanned for the 3-D brain model, the screws show up on the scan, creating stable reference points to work from, much the way GPS satellites work. The team can triangulate any spot in the brain using three screws. Four is better, to prevent ambiguity, and five — the number I get — is belt-and-suspenders solid. During the surgery, you can move and talk, because when your head moves, the reference screws move with it. A small robotic insertion device is clamped directly to your head with more screws, effectively turning your skull into the support frame.

**1 Correction, Fri March 1 06:00:00 EST 2007**

*The first US surgery to place stimulators directly in the subthalamic nucleus took place at Mt. Sinai Medical Center in New York, not Cedars-Sinai Medical Center in Los Angeles, as originally reported. ([Return](#) to the corrected text)*

This approach also means that after the initial scan, I get to go home, giving the surgeons the afternoon and evening to plan my operation. Instead of being locked into a metal brace, I sit on the couch sipping Chardonnay and eating Vicodin — five titanium bolts jutting from my skull.



**Rewiring the Brain**

To treat Parkinson's disease, deep brain stimulation uses a pacemaker the size of a deck of cards implanted under the collarbone to deliver continuous low-voltage shocks down two sets of stiff wires to electrodes near the subthalamic nucleus, a peanut-sized cluster of neurons near the center of the brain. The electrodes can be turned on or off in various combinations to increase or decrease the size of the area being stimulated. The idea is to correct errant impulses that result in the loss of motor control.

one of the chief dangers of deep brain stimulator surgery. My last moments will be in this Stanford hospital room, looking at a stain on the ceiling above the GE logo on the scanner.

But no. After an agonizing 20-minute wait, the anesthesiologist and the nurse return, kindly looks on their faces. Fine. Everything is fine. No bleeding. No problems. It most likely hurt because the local anesthetic wore off, and the surgeon touched the margins of the scalp wound while trying to position the probe. The issues were actually relatively minor, they assure me, and well within the bounds of normal operating procedure.

Hiccups happen. In this case, the doctors suspect that the brain shifted a millimeter or so. Things weren't quite where the model said they should be. This can result from either loss of cerebrospinal fluid or simple agitation. It's why they usually do the two sides of the brain a week apart, with fresh scans each time. They can finish the other side later, they assure me, no problem. Next week, or the week after.

In the days after the surgery, my Parkinson's symptoms are remarkably diminished. This is called the microlesion effect. Apparently just the swelling from the poking around is enough to make things better for a while. It fades, but it's awfully encouraging. For about five years now, I've been living without hope. This is a nice change.

**No one really knows** precisely why deep brain stimulation works. Some things about the deep brain structures, like the thalamus, are understood well enough for stimulators to be routinely successful. But the high-level brain structures in the neo-cortex, where all the evolutionary action has been for the past 100,000 years or so, are still largely a mystery. How does shocking the thalamus in the deep brain help the cortex in the upper-level brain control fine motor movement? Is this suppressing electrical activity or enhancing it?

For the second surgery, I agree to do my part for science, volunteering for a battery of brain tests while they have my hood up. Before the procedure, Henderson shows me a little gold grid, about half the size of my fingernail. He will lay this grid on my cortex, and it will register neurons firing as the doctors have me perform simple exercises. "It has 100 wires," he says proudly.

I try to look impressed, but I'm thinking, "Only a hundred wires?" To be fair, the hundred wires are actually 100 silicon microprobes (each 0.06 inch long) packed into a 0.16- by 0.16-inch grid. When the grid is implanted into the cortex, each microprobe records the activity from at least one neuron, and sometimes as many as three or four. Right now this is the maximum amount of information we can extract from the human brain.

**Things aren't** going as planned. Lying on the table, I'm starting to get very worried. The second electrode still doesn't sound right.

Then something wonderful happens. It's hard to describe, but for more than five years my right hand hasn't felt the way it should. Suddenly, it's back. I can tap my fingers, move freely. It's the miracle cure for Parkinson's I've been reading about! I tell the neurologist.

She seems unconvinced. I'm saying they've hit the sweet spot, but it may be that they've hit the wrong sweet spot. There are structures near the subthalamic nucleus that affect mood, and the doctors don't want to place an electrode there. They aren't trying to make me happy, like some lab rat with an electrode implanted in its pleasure center; they're trying to cure my Parkinson's. "You feel euphoric?" she asks.

"No, no," I say. "It's just that my hand, my hand is back. It's been years since it felt right."

"And this makes you feel how? Happy?"

The rest of the team starts making grumpy noises. The neurosurgeon calls for another electrode, but the physicist assures him that's not the problem. I feel tired and worried. I mention this to the neurologist.

"He has feelings of imminent doom." Well, I don't know about imminent doom, but ...

The neurosurgeon tries something. It hurts like a sonofabitch. Ow. Ow! I have no idea what's going on; I didn't think it could hurt — there are no pain receptors in the brain. Is this a stroke? Am I dying?

The doctors decide to stop the surgery. They staple me shut and cart me down to the CT scanner. This must be a stroke, I think,

It's neat-looking and compact, but my first Apple II computer had 1,000 transistors in that space, not 100 wires. It wasn't long before my PC had a processor with 100 million transistors. Just 100 wires? It's a reminder that this technology is still in its infancy.

After the experiments, the second surgery goes about as smoothly as possible. No sooner do I stick out my tongue and tap my fingers a few times, it seems, than it's done. In record time.

They test the electrode placement by putting a little voltage through the wires. There's a ferocious buzzing, like a swarm of bees in my head. They try a few modulations, and the buzzing goes away.

Finally, the anesthesiologist cranks up the gas, and I'm off to never-never land while the surgeon runs the wires under my scalp, places the pacemaker under my collarbone, and closes me up. They had planned to do the pacemaker later, but things have gone so quickly that they do it now.

I wake up as they wheel me into recovery, which at Stanford is a kind of fun house sideshow. People in various states of undress — many of us having just had parts removed or new parts installed — loll or roll about in pain and confusion, all under the watchful eyes of a room full of nurses, orderlies, and aides. The occasional doctor breezes through to provide expert advice or — because this is a teaching hospital — comic relief. The nurses, rolling their eyes, patiently guide the young doctors like sergeants working with newly minted lieutenants.

The pacemaker itself hurts more than I expected. It feels — and looks — like I've been stabbed in the chest. There's clearly no room under my collarbone for this thing, and it bulges out like a first-generation iPod in a tight shirt pocket. The wires aren't the little hair-thin fibers that I expected, either. They're as thick as speaker wires. Which makes sense, because they've got to take a lot of wear and tear without breaking. But the whole thing is more obtrusive than I realized it was going to be. And more painful.

A month after the second surgery, I'm back at Stanford to program the stimulator. Getting the settings right is midway between an art and a science. On each side of the brain is a probe with four electrodes. The team needs to decide which electrodes to activate with how much voltage. The device is capable of delivering 10.5 volts, but at that power there's danger of damaging the brain tissue. So we start at 2 volts and won't go over 3.5.

Raising or lowering the voltage changes the size of the area being stimulated. If the electrode is too near a structure like the internal capsule, the stimulation can cause muscle contractions; too near the substantia nigra, it causes hypomania or depression. Turning the voltage down reduces the affected area so it doesn't cause the side effects, but it makes the whole device less effective.

If necessary, doctors can activate two electrodes so the current flows from one to the other, rather than from the electrode back to the pacemaker in my chest. This drastically shrinks the affected area.

Ultimately, getting the system to work right comes down to trial and error. There are 1,200 possible settings, and fatigue alone prevents testing more than a few at a time. The team starts by trying each electrode on each side. Then they click up the voltage until my tongue sticks to the roof of my mouth, back it down until I feel nothing worse than a slight tingling, all while testing me for Parkinson's symptoms by having me tap my fingers and twirl my wrists as if I were beating eggs.

We hit the sweet spot on both sides at 2.5 volts. I can tap my fingers and scramble eggs like gangbusters, with no side effects. I take a Parkinson's test and ace it. I have no observable signs of Parkinson's except for a tendency to fatigue rapidly. I walk out of the hospital, click my heels in the air, pick up my new fiancée, and swing her around. It's the happiest day of my life.

Over the next 24 hours, my symptoms return. Henderson tells me to try increasing the voltage by using the remote control he gave me and to add some Parkinson's medication to the mix. I'm able to get good symptomatic relief, but there are other problems. For starters, I have to turn the device way down to sleep. And I can't tell a joke — my timing is off. My natural gift for mimicry is also gone, as it seems I've lost some of the fine control over my vocal cords. I'm hesitant in social settings: By the time I can muster a response, the topic of conversation has moved on. I'm slightly out of phase with everyone I talk to. And I can't write worth a damn.

At first, the neurology team has a hard time zeroing in on the problem. They can't test for the impairments I'm experiencing, and since none of them can mimic an accent or tell a joke properly either, they don't have much to go on.

Finally, after three months of tinkering, I find another neurologist, Eric Collins, who gets it. He has me count backward from 100 by sevens. With the device off, no problem. With it on, I can't do it. We change the settings until I can. We have to go to two active electrodes on the right side instead of one. He has me recite poetry from memory and fine-tunes me again. Better, almost there, but I'm too tired to continue. And I still can't write. It's like being in a fog.

I email Henderson, describing the problems and the changes the new neurologist has made, and he suggests reversing the polarity on the right side. He knows what he's doing and it helps — a lot. I request that they go to two electrodes on the left side as well. Bingo. After these changes, my head clears. The fog begins to lift.

Today, eight years since the first signs of Parkinson's and after months of fiddling, my body is almost free of symptoms. With the stimulator turned off, a Parkinson's test shows 20 significant impairments. With the stimulator on, it drops to two. Add just a touch of L-dopa and it drops to zero.

The last wisps of fog have cleared away. My jokes make people laugh again. I can keep up with conversation. I can ride a bike. I can write. It's been five months since the surgery, but it has finally all come together: It works. I forget that I even have Parkinson's most of the time. And last November, I went back to work full-time. It's a miracle. A second chance at life.

I know it's not a cure. Parkinson's is degenerative. Those neurons in the brain keep dying, producing less and less dopamine. How long will I feel normal? No one knows. A long-term study completed in 2004 showed that four years after surgery, patients still typically required 50 percent less L-dopa than they did before.

After that, we'll see. The surgery has had FDA approval only since 2002. The long-term effects are simply unknown — I'm the guinea pig. The trick now is to make the most of the time I've been given.

Hand me that bar of surf wax, will you? I haven't taken this board out in a long time, and the Internet is forecasting 6- to 8-foot swells, with clear skies.

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