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How to mend a broken mind; What does sadness sound like? 'Cells firing five to 30 times per second,' and making it stop is a matter of 'location, location, location,' says the surgeon leading a team of Canadian pioneers who are restoring the lives of the deeply depressed. Their results are so promising that researchers are already trying the procedure on an array of other disorders. Globe and Mail medical writer Carolyn Abraham and photographer Charla Jones uncover the magic of deep brain stimulation

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The first time I met Sean Miller, we were strangers waiting in a corridor at the outpatient psychiatry unit of Toronto General Hospital. He was the redhead, wearing a grey sweatshirt, jeans and a 100-watt smile. "Popular place," he said.

He looked rosy and energized, as if he had been for a run. "Pretty warm out there today," he added. He mentioned rain in the forecast and cracked a joke about the "nice weather" we had been having. Then a door opened down the hall and he waved goodbye - "See ya!"

A few minutes later, Peter Giacobbe, a 33-year-old psychiatrist, beckoned me to his office. "It's fine," he said. "You can come in."

I had been waiting to observe Dr. Giacobbe's 4 o'clock emergency appointment. Emergencies are routine in psychiatry. Patients turn up worried about a medication, feeling manic or fighting off suicidal thoughts.

But that May afternoon was something different: A 41-year-old patient had placed an urgent call to have his battery checked. His depression had been so severe that last year he allowed doctors to drill a hole in his head and thread two battery-powered electrodes down into his brain. The operation made him the 21st subject in one of the more radical mood-altering experiments on the medical books - a world-first, Canadian-led trial to treat depression with a procedure called deep brain stimulation.

The man had visited a lawyer friend at a courthouse, passed through a security check and later felt a downswing in his mood. Had the metal detector somehow short-circuited the electrodes in his head?

Dr. Giacobbe opened his office door and that was the second time I met Sean Miller.

He laughed and tapped the top of his head. "Yeah, well, I was depressed - before this went in," Mr. Miller said. "This thing saved my life."

At a spitfire clip, he described the way he now

bounds of out bed in the mornings, impatient for the day. "Before the operation, I wasn't myself. ... I love life, seriously love it, but I couldn't think straight. I couldn't work. I hardly left my apartment for four and a half years."

"You're the happiest person I've met all day," I told him, and meant it.

"I know," he beamed. "Isn't that crazy?"

From the home front to the workplace, from the schools to the streets, mental illness presents one of the great challenges to modern society, a leading cause of disability, absenteeism and deaths due to suicide. Not only does it strike one in five Canadians, usually in their prime, but too often it defies the ability of modern medicine to treat it.

Depression, which affects one in 12 people in this country, is one of the trickiest disorders to cure. While 80 per cent of patients find effective relief with standard drug or psychotherapies, the latest numbers suggest that only 40 per cent truly feel well. Worse, experts estimate that, for 10 to 20 per cent of sufferers, nothing works.

To the shock of many, and the horror of some, the most promising treatment for intractable depression on the horizon is not a designer drug, a new form of talk or even genetic therapy. It's electricity. The same force that powers our TVs and microwave ovens can lift the human spirit.

With deep brain stimulation (DBS), surgeons implant metal rods that aim steady pulses of electrical current at the faulty neural circuits believed to underlie mental illness. Spaghetti-thin, the rods connect to a cable that snakes invisibly down the neck to a cookie-sized, battery-operated regulator embedded just south of the collarbone.

DBS itself is not new. Doctors have used it to treat physical ailments for nearly 60 years, first to counter chronic pain and since the 1990s as a therapy for movement disorders. But society has long separated neurological diseases from psychiatric ones, as

though physical conditions can stem from concrete malfunctions of the brain but maladies of the mind cannot.

Then in 2003, working with just six patients, University of Toronto researchers tested DBS on depression. It not only proved safe, it also made four of them better. Since then, 50 patients in Toronto, Vancouver and Montreal, as well as at least 30 in the United States, Europe and South America, have undergone the procedure in a bid to see whether electrical implants can indeed mend a broken mind.

The Toronto trial, open only to people whose depression has proved impervious to all other treatments, so far suggests that DBS is safe and offers lasting relief in more than half of all cases. The early results are encouraging enough that one manufacturer of the DBS device has already started down the road to have the U.S. Food and Drug Administration officially approve it for treating depression.

"The emerging picture seems to be that, if you can get better [with this], you can stay better," says neurologist Helen Mayberg, whose work at the Baycrest Centre's Rotman Research Institute in Toronto laid the groundwork for the DBS trial. Ivy League researchers in the U.S. are now investigating DBS as a treatment for obsessive compulsive disorder and, at Emory University in Atlanta, where Dr. Mayberg is now based, the target is type 2 bipolar disorder.

Shocking the brain to behave is hardly a revolutionary concept. Doctors first tried it in the 19th century, and in 1937, Italian researchers launched electroconvulsive therapy, zapping patients' heads to induce seizures that sometimes improved symptoms, but also damaged memories and muscles. Even now, a gentler version of ECT remains an established, if controversial, treatment for a narrow range of severe mental disorders, depression in particular.

But the Toronto researchers point out that it's not the use of electricity that makes their treatment a major advance - it's where they put it. "With brain surgery, it's like real estate - it's location, location, location," says Andres Lozano, the neurosurgeon and senior scientist who has led the trials at Toronto Western Hospital.

DBS offers a fresh opportunity to "de-stigmatize" mental illness, he says. If a mechanical device can regulate mood, then "behaviour is modulated by the same kind of circuitry. ... People have no control over it. ... They can't just 'pull up their socks.'

"There has been this distinction between neurology and psychiatry that's artificial and arbitrary."

But brain surgery for psychiatric conditions has a long, unhappy history - from head bashing in the Bronze Age to the 20th century's infamous frontal lobotomy. After psychopharmaceuticals hit the market in the 1950s, cutting as a treatment for mental conditions became as unfashionable as Brylcreem. Which makes it all the more unlikely that any

depression treatment involving drills and electrodes is making such an auspicious comeback.

"Some people say this is barbaric - One Flew Over the Cuckoo's Nest kind of stuff," Dr. Lozano adds, but more than 40,000 Parkinson's patients have already had DBS ease their tremors by targeting parts of the brain where motor neurons misbehave.

"People have no problem operating for Parkinson's, but they have a problem operating for psychiatric conditions," he says, adding that "we can go anywhere in the brain now. We can turn it up, we can turn it down regulating it, just like a thermostat."

The only difference in using DBS for depression is that the electrodes target the brain area where sadness lives.

'I LITERALLY FELL APART'

A few weeks after we met at Toronto General, Sean Miller sits in a Yorkville café. He downs a bottle of water and shrugs - nothing from his childhood predicted his long spiral into despair, he says.

He had grown up happy in Toronto's tony Rosedale, the second of three children in a warm, supportive family. His father ran an import-export business. His mother, a former social worker, stayed home to raise the kids. He had close friends, attended good schools, flitted off to camp every summer, skied, played tennis and flirted with serious hockey.

He faced his only obstacle at 14, when he developed Guillain-Barré Syndrome, an autoimmune disorder that temporarily paralyzed him. He spent a year in rehab centres. When he returned to school, with a dropped foot and an awkward gait, he could no longer play hockey. Even so, he says, "I felt frustration and anger, but not depression."

He did his last year of high school in the south of France, graduated from university to an exciting film industry job and landed a serious girlfriend. Life was grand.

But at 24 he had his first bout of depression. It was mild, but left behind a sense of "joylessness ... purposelessness." A psychiatrist prescribed an antidepressant but he found the libido-killing side effects too much to bear. He quit the medication after a year.

The next episode, at 27, was tougher to beat. He left his girlfriend and his job and flew to Thailand for an indefinite stretch of travel. While there, he started smoking dope, which he suspects "changed the depression from feeling low to something based on fear and anxiety."

He returned home, resumed medication and, eventually, went back to work.

In a bid to avoid a relapse, he regularly attended 10-day meditation retreats, trying to train his mind "to stop the stream of negative thoughts." He even volunteered to help others stay positive, answering

the phones at a distress centre.

He remained well into his early 30s, climbed corporate ladders in sales and marketing and became involved in another serious relationship. Then, once again, he stopped taking the medication.

"I know, it was crazy," he says, laughing now at what he did. "The side effects bothered me - but also, I was kind of a health-conscious guy and I didn't want to take drugs."

But at 36 his depression returned and this time, the third time, the drugs proved powerless. "I literally fell apart. The next four years were the worst of my life."

Most friends stood by him. His girlfriend at the time rarely left his side. "But there were a few, who would be like, 'Sean, get a job get a life ... get your ass out of bed.' I didn't even feel like I was a part of life," he says. "It felt like being buried alive."

WELCOME TO AREA 25

Sadness lives behind the eyeballs, four centimetres back in from the forehead. That's where Dr. Mayberg found it after 20 years of brain-imaging studies, in Boston, Texas and then Toronto in the late 1990s.

The pictures showed that a patch of the prefrontal cortex known as Brodmann Area 25 flicked into high gear when healthy subjects were made to feel sad, for example, by reading a personal essay about losing a loved one. At the same time, significant swatches of the subjects' frontal cortex, the brain's chief executive officer - its motivator and decision-maker - powered down. When their minds moved away from sad thoughts, the cycle reversed. Activity shut down in Area 25 and shot up in the frontal lobes.

But in patients with depression, the cycle never shifted. The lights at Area 25 were always on, stuck in a constantly active mode, compromising cognition in the frontal cortex.

Sitting in the ancient limbic lobe passed down from our slithering ancestors, Area 25 connects to the brain structures involved in human function - emotion, memory, stress, sleep, libido, appetite, energy levels and learning. "It's linked into all the core areas involved in depression," Dr. Mayberg says.

The images led to a hypothesis: If they had found one of the sites where a feeling runs amok, could they find a way to fix it? Would the type of DBS used for Parkinson's charge the cells in Area 25 out of their "on" position?

In 2001, in a moment of serendipity, Dr. Mayberg met Dr. Lozano at a conference of neurosurgeons.

Dr. Lozano was world renowned for his brain-stimulation operations. He had performed DBS for Parkinson's and other neurological disorders since 1992 - about six times a month. When Dr. Mayberg suggested that they try it for depression, he thought it was "a long shot" - but right up his alley. "I don't want to do the ordinary, the routine, the established,"

he says. "I'm not a fan of incrementalism. I just want to take big steps."

A HOLE IN THE HEAD

In the spring of 2006, in the grip of depression in his downtown apartment, Mr. Miller watched a television segment on the DBS procedure. His mother had called to tell him to tune in.

By that point, he had burned through 20 types of antidepressants, five months of cognitive therapy and four rounds of ECT. He had been admitted to hospital three times for two-week stretches. He had tried meditation, acupuncture, vitamin regimens and a shop's worth of naturopathic remedies. He had changed his diet and stopped eating dairy. His parents had even spent \$4,000 so he could undergo transcranial magnetic stimulation, an experimental treatment that uses rapidly changing magnetic fields to alter the brain's circuitry. None of it helped.

"I was suicidal every single day," he recalls, "but I was scared shitless to die too."

On the Internet, he researched painless ways to kill himself and wrote a suicide note in the event he could ever bring himself to do it. It told family and friends there was nothing anyone could have done, that he loved them and that he was sorry.

Until he saw the DBS segment, he did not hold out a glimmer of hope that he could ever recover. The patient featured was just like him. She had tried everything and everything had failed. Then, after doctors turned on those electrodes, she finally emerged from her long black fog.

As radical as brain surgery seemed, Mr. Miller knew instantly that he wanted to be a test subject. Having been paralyzed as a teen, he had often thought of tradeoffs he would be willing to make to be free of the anguish. "I used to lie there and think, 'I'd give up an arm, or a leg, or both my legs ... I would take paralysis over depression any day of the week.' "

Fear, he says, drove him to seek DBS. "It wasn't having the guts to do it - it was what would happen if I didn't do it."

Having a hole drilled in his head seemed a small sacrifice.

'MY LEGS ARE ON FIRE'

On a May morning in operating room No. 6, Dr. Lozano peers down at a patch of scalp, shaved and stained rusty red with iodine. He picks up a blade, cuts a square and tugs back the flap of flesh.

"Okay, John, you're going to hear some noise now. It sounds like an air gun at Canadian Tire, the type they use to take the nuts off your tires," he says, powering up the drill.

It takes two minutes to pierce a stubborn centimetre of cranium and bore a hole the size of a nickel. A nurse asks if the patient feels okay. He gives her a

thumbs up.

Patient John McCutcheon, 38, doesn't have a mental disorder, but he is still a pioneer - just the second person with multiple sclerosis ever to undergo DBS in a bid to ease the phantom-like pain in legs he can hardly feel.

"I've woken up dreaming my legs are on fire," he told Dr. Lozano before the surgery began.

"What is it on a scale of 1 to 10?" Dr. Lozano asked.

"10-plus."

Mr. McCutcheon's head has been immobilized by a thorny titanium crown screwed into his skull. A chrome cradle grips his neck like a pipe in a vice. The probe that will slide through the hole in his skull sits locked in an arched frame that stretches over his head like a steel rainbow. The entire contraption makes him look part person, part metal, and wide awake - as he must be, to tell the surgeon what he feels as the probe plunges 8.5 centimetres into his brain.

First, it will journey to Mr. McCutcheon's thalamus, to explore the rebel neurons scorching his lifeless legs. The sensory circuits near the midbrain will be the second destination, as the probe confirms exactly where the electrodes should go.

But for Dr. Lozano, every DBS procedure is about more than implanting electrodes - it's an opportunity. Every dive beneath the brain's glistening folds is a chance to glean its secrets, and often he has.

He discovered how neurons that once governed limbs that are now gone can misbehave to cause phantom pain, or take up new jobs to control other body parts. He found mirror neurons, the cells responsible for empathic pain, which can make you close your eyes or turn away when someone gets a needle. In January, while operating on an obese patient, he stimulated part of the brain that controls appetite and came across a crucial new area involved in memory. Expected to talk about food urges, the man instead vividly recalled a date he had had in a park more than 20 years ago ... right down to what he and she were wearing.

As a result, Dr. Lozano has launched a pilot study to see whether DBS can improve the memory of early Alzheimer's patients. In the process, the Spanish-born neurosurgeon - whose fit, six-foot-plus frame seems to tower over everything - has become a celebrity scientist at 49 (the hospital's public-relations director calls him the resident rock star), featured in *The New York Times*, *The Independent* and *60 Minutes*. Patients come from as far away as the Philippines to have him operate, and doctors move to Toronto for year-long stretches to watch him work. This particular morning, it's a surgeon from Singapore and another from Manhattan.

Up in his office, with his bookcases and antique surgical devices that have the feel of old mariners' instruments, Dr. Lozano likens himself to an explorer

- to Christopher Columbus, he says, "describing the frontiers of the brain."

"I want to go where no one else has gone before," he says, without irony.

THE SOUND OF SADNESS

The hands of a surgeon usually steal the show in an operating theatre. But with DBS, the ears play the starring role. The micro-electrode probe that descends into the brain one micron (a millionth of a metre) at a time detects the electrical signals in the tissue it penetrates.

Electrophysiologist William Hutchinson operates the probe, which is wired to a bank of audio-visual tracking equipment that lines the rear wall of the operating room like components in a stereo shop. There are oscilloscopes that display volts in visual spikes, amplifiers that translate the firing pattern of a single neuron into sound, suddenly filling the room with rhythmic pings and rat-tat-tats like eerie signals from a distant planet. Everyone falls silent, eavesdropping on the alien within.

They begin to sample the sounds of Mr. McCutcheon's neurons 10 millimetres above the target in the thalamus. The neurons talk and the probe talks back, emitting a low-voltage current to elicit a response, and the cells can do one of two things: cease or fire.

"John, we're going to put some electricity into your brain now," Dr. Lozano announces. "You'll hear a beep. Tell us if you feel something."

After a zap several millimetres north of the target in the thalamus, Mr. McCutcheon reports sensation in his cheek, then his jaw, then somewhere around his ear.

"Okay, onward," the doctor says, and the probe heads farther south to the cells that once moved his legs.

Periodically, Dr. Lozano puts his hands on Mr. McCutcheon, scratching his chest, poking his hip, patting his leg as he listens for the neural response his touch might trigger.

"Cells make different sounds in different regions. They're like a guide; they tell you where you are in the brain," he says. "It's like driving through Europe. ... You know where you are by the language they speak."

Neurons that control vision fire at different rates than those that control movement. Some cells are idlers. Others burst and pop like the backbeat on a jazz track.

And how does sadness sound? "Cells firing five to 30 times per second," he replies.

In DBS operations for depression, Dr. Lozano runs a show-and-tell. Instead of touching patients, he vies for emotion. He has them read moving stories or shows them pictures, scenes of splendour, or

violence, images of despair or a sexual nature. He asks how it makes them feel, focusing on their words as well as the noise their neurons make.

But motion or emotion, the method is the same, he explains. When he tells Mr. McCutcheon to try to move his right foot, for example, a cell fires fast in the millisecond before the attempt. "Okay," he says, "so that's involved in planning the movement."

The erratic sound of the misbehaving neurons ring clear - like static from a radio in need of tuning. "His neurons are firing abnormally, and we want to turn them down," Dr. Lozano says. "It's causing a brainstorm in the pain pathway."

A few moments later, he reaches the target deep in the thalamus and signals Dr. Hutchinson to charge the probe. Mr. McCutcheon says it makes his legs tingle from hip to toe. "This might be a good spot" to place the first electrode, Dr. Lozano says.

They move next to strike the second target in the midbrain, the periaqueduct, where sensory circuits control the emotional response to pain - involved when a soldier fights on, oblivious to an injury, say, or when an athlete keeps playing despite a broken bone.

As the probe slides down, it passes cells that seem strangely quiet. "Silent neurons," Dr. Lozano says, "terra incognita" - no one knows what they do, and electricity seems to have no effect on them.

A moment later, he steps away from the patient to whisper a prediction: "When we reach this target, he's going to tell us he feels good. ... Some people say, 'Oh, I feel calm, mellow, like I had a double scotch.'"

"Go," Dr. Lozano says, directing Dr. Hutchinson to charge the probe.

"How does that feel, John?"

Suddenly, Mr. McCutcheon's face relaxes: "Oh, what did you do? That feels good."

Dr. Lozano asks if the feeling reminds him of anything.

"Like when the kids were born" is the reply.

Bingo. This will be the site for electrode No. 2.

The sensory circuits in the periaqueduct happen to be directly connected to Area 25 and the instant well-being Mr. McCutcheon felt when they charged it, Dr. Lozano says, was the same response from the first patient who underwent DBS for depression in May of 2003. "She suddenly said, 'What have you done? The room is in colour.'"

REGROWING THE BRAIN

With depression, the electrodes seem to quiet the hyperactivity of Area 25 like a muzzle on a barking dog. Yet scientists suspect that the story is more complex.

Dr. Lozano, who grew up in Ottawa and holds the Canada research chair in neuroscience, estimates that the currents directly affect up to 20,000 neurons, but flow outward "like dropping a pebble in a pond." Research suggests it may have an impact on the very structure of the brain.

In the mid-nineties, University of Calgary cell biologist Samuel Weiss discovered that the adult brain can actually produce new cells. Since then, some researchers have come to believe the steady growth of new brain cells may be crucial to mental health.

For example, imaging studies show that people with depression have a smaller hippocampus in their brains than healthy people do. Psychiatrist Glenda MacQueen, head of the mood disorders program at McMaster University in Hamilton, recently reviewed the brain images of more than 1,000 people with depression and 1,000 healthy control subjects, and found the hippocampus to be especially small in those who had suffered several episodes of depression.

Housed in the limbic lobe along with Area 25, the hippocampus is best known as a mansion of memory - the great neural archive that records the context of our lives. But it has also become a hot property in mood studies.

People with depression have long reported problems with memory. As well, half of people with depression have high levels of stress hormones circulating in their blood and it is the hippocampus that controls the chemical cascade that stress triggers. (When the brain mistakes a ruffling curtain for a tiger ready to pounce, it's the hippocampus that says, "Relax, it's only a cat," Dr. MacQueen explains.)

Stress hormones, meanwhile, are particularly toxic to cells of the hippocampus, which may explain why the structure shrinks with depression. In animal studies, Dr. Lozano and colleagues have discovered that DBS can boost new brain-cell growth - particularly in the hippocampus. Neuroscientist Scellig Stone, who works with Dr. Lozano, has found that one hour of deep brain stimulation in a rat doubles its production of new cells.

Dr. Weiss speculated that depression that responds to therapy or medication may be the result of chemical imbalances built up over the short term. But deeply rooted depression may be more responsive to DBS if the procedure really does boost brain-cell growth.

Although Dr. MacQueen has tried to study the hippocampus size of depression patients before and after DBS, images taken so far have not allowed accurate measurements. For now, researchers must base their results on what the patients tell them.

PROS AND CONS

Through 2006, Mr. Miller imagined his electric moment - lying on the operating table, doctors

flicking a switch and saving him. He had called his psychiatrist for a referral to the trial as soon as he saw the TV segment. Then he lobbied, pleading his case to the doctors running the trial, phoning and writing letters.

But he wasn't alone. Results from the initial experiment made headlines around the world in 2005, and nearly 700 requests for DBS poured in. Even now, the waiting list has more than 30 patients.

Deciding who makes the cut is in part the job of Sidney Kennedy, the health network's head of psychiatry. Deeply involved in planning the DBS trial, he describes the procedure as a "major paradigm shift" in the treatment of a mood disorder. "It has been an interesting role for the psychiatrist: He's evolved from psychotherapies, to pharmaco-

therapy ... to adjustments with stimulators. ... It's one of the best examples where psychiatry meets neuroscience."

Dr. Kennedy, 57, had no great expectations when the trial began. Even after the initial heady results, he tried to wear "the hat of the skeptic." But "I thoroughly believe now there are no five-year placebos," he says (referring to how long the first patient has had relief of symptoms). "I do think a cycle of depression continues for these people, but it's not as severe."

Not that DBS is without its critics. For example, Jeffrey Schwartz, a renowned research psychiatrist at the University of California at Los Angeles, a leading proponent of cognitive behavioural therapy and co-author of *The Mind and the Brain: Neuroplasticity and the Power of Mental Force* has called DBS "essentially nothing more than an electrical prefrontal lobotomy."

He told a U.S. newspaper that its pioneers have been careful, but that he worries its widespread use could lead to abuse by companies or amateurs offering it to anyone who wants to tune up his mental state.

In response, Dr. Lozano stresses that, unlike other psychosurgeries, DBS can be reversed, the electrodes removed, and five years since their first patient, none has suffered serious side effects.

Dr. Kennedy says he suspects that it does not work for all patients because, like faces, no two brains are exactly alike. Different brain regions could be involved in depression in different people, he explains. "Maybe in 30 years, people will look back and say, 'How primitive - they stuck electrodes in their brains and turned the batteries on.'"

Still, all surgeries carry a risk, Dr. Lozano notes. The experience with DBS for Parkinson's suggests that one in every 500 patients will suffer a hemorrhage during the surgery. Four in a thousand will suffer a serious complication, such as a permanent neural deficit or even death. If the numbers of patients being treated rise appreciably, "it will happen" for depression as well, he says flatly. "It is just a matter of time."

Even the positive affects rarely appear right away. A few patients report relief as soon as the electrodes have powered up. But for most, it takes weeks, even months, to find the right voltage and frequency - "the sweet spot," as they call it.

After the operation, Dr. Kennedy and Dr. Giacobbe, their offices mere steps apart, see each patient once a week to track their progress and tweak their settings. As time passes, the appointments are less frequent, but they still require adjustments.

Unlike patients with pain, those with depression are not able, or allowed, to adjust their own voltage. For one thing, researchers say the electrodes should be on all the time. Adjusting them haphazardly could have negative effects.

"We're managing this ever-growing cohort," Dr. Kennedy says, which at the moment includes 30 men and women from their late 20s to their 60s. "We haven't had people very often who couldn't tolerate the stimulation. ... If it's up too high, they feel an inner restlessness, you know, 'wired,' and turning it back down relieves that."

Even when they do find their sweet spot, Dr. Giacobbe says, it can be difficult for people who have been profoundly depressed for so long suddenly to reclaim their lives. "They still have ups and downs," and even their relationships change. One patient grew frustrated with a partner who missed the needy and vulnerable homebody he had been when he was sick.

"In a way, this is like learning to walk on a new hip," Dr. Giacobbe explains. "I help them adjust and I adjust them."

AT LONG LAST RELIEF

After nearly a year of lobbying, doctors eventually decided that Mr. Miller fit the criteria of treatment-resistant depression. In February, 2007, a metal crown bolted to his temples, he at last found himself on the operating table.

But he did not have his electric moment then and there. He awoke from the procedure, groggy, sore and "deeply depressed." A technician arrived at his bedside to switch on the stimulator, and he felt ... nothing. "I was so upset. I went home devastated."

He began to suspect that the treatment had failed, but Dr. Giacobbe gave him regular "pep talks" and, over several weeks, slowly increased the voltage. At month five, and nearly seven volts - about enough to power a smoke detector - the black fog finally lifted.

"I just woke up one morning and I felt good. I actually wanted to get out of bed. Ah, and I was hungry, I was so hungry - I couldn't wait to eat." He popped out to a deli had a Reuben sandwich for breakfast.

"I called my friends. I called my mom. I was, I don't know, excited. I felt the joy of being alive."

In the past year, Mr. Miller has rebuilt his life, visiting friends, playing sports and launching a business. But he has had his low points too. His father died of cancer last spring before he could see his son free of depression. Somehow the grief didn't knock Mr. Miller back into the darkness. But certain symptoms return - sudden flashes of anxiety, trouble sleeping.

Dr. Giacobbe says patients can have their moods improve, but still have a lazy libido or erratic appetite. Sometimes such symptoms seem like warning signs that the treatment is failing - which is what happened to Mr. Miller after he went through the metal detector at the courthouse.

It seemed a reasonable concern - doctors give DBS patients exemption letters to use at airport security - but at the emergency appointment, Dr. Giacobbe reminds him that it can be tricky to distinguish depression from a mere mood swing.

"It's hard when you've been sick for so long," Mr. Miller says. "You have to remember that every bump in the road is not a return of the depression."

"Okay, so let's take a look," Dr. Giacobbe says.

Mr. Miller pulls up his sweatshirt, exposing his chest, and looks down to the slight bump of his battery pack. He says he had joked with his fitness trainer that he would have to work out the "pecs" on the opposite side a little harder "to make it even."

Dr. Giacobbe aims a remote control at the power-pack buried in Mr. Miller's chest and flicks through settings like he's changing TV channels.

"You're at 6.75 volts," he says. "I'm keeping it there."

"Am I the highest patient you have?" Mr. Miller asks.

"No, there's another patient around seven."

"You don't want to turn me up?" Mr. Miller asks, laughing.

"No," Dr. Giacobbe says. "You're good."

Carolyn Abraham is The Globe and Mail's medical writer.

Tapping the brain

Led by Dr. Andres Lozano, the Toronto surgical team prepares multiple sclerosis sufferer John McCutcheon for an attempt to use deep brain stimulation to ease the fiery phantom pain that plagues legs he can otherwise barely feel. He is only the second MS patient to undergo the treatment. Once Mr. McCutcheon is in position, his head is covered, secured and fitted with the 'stereotactic' frame used to guide the equipment that will bore a hole the size of a nickel in his skull and send a micro-electrode probe into the depths of his brain.

Now the electrodes are being deployed in much the same way to hunt down the regions of the brain whose malfunctioning is responsible for mental illnesses, such as depression.

Once the probe begins its descent, the doctors must listen closely as sophisticated audio equipment tells them how the device is interacting with the brain's neurons, information that is also displayed in graphic form. From time to time, Dr. Lozano, above, touches the patient, scratching his chest or patting his leg to see what response his touch may trigger. 'Cells make different sounds in different regions ...,' he says. 'It's like driving through Europe. ... You know where you are by the language they speak.' When operating on depression patients, the neurosurgeon, shown above out of surgical garb, tries for emotion instead. He has them read stories or shows them pictures and then asks them how they feel, as he listens to the sound their neurons make.

Brain food

Brutal cut

Egas Moniz, the Portuguese neurologist who invented the prefrontal lobotomy, earned the 1949 Nobel Prize in medicine after proving he could calm behaviour by cutting out a patient's frontal lobes. The so-called "white cut," which U.S. surgeons later performed with ice picks, left a legacy of apathetic automatons, suffering from incontinence, epilepsy and confusion.

Fire power

Researchers say deep brain stimulation boosts the brain just as a pacemaker pumps the heart. But the human body has only one heart that beats roughly once per second. The human brain has 100 billion neurons, any one of them firing up to 130 times per second.

Depressingly small

In depressed people, the brain's hippocampus - repository of our memories - tends to be about 10 per cent smaller than normal. In the worst cases, in particular those linked to post-traumatic stress disorder, the deficit can be 20 per cent.

Current events

The lowest DBS setting thus far in the Toronto trial fires at two volts, with seven volts the highest. In contrast, a neuron fires at one-millionth of a single volt. Most people in the trial are in the three-to-four-volt range, a setting that should provide a five-year battery life.

Carolyn Abraham

Surgical brainwave

In deep brain stimulation, doctors implant metal rods emitting electrical pulses to try to treat depression.

THE OPERATION

1. Exact co-ordinates of the target are mapped in 3-D with an MRI.
2. Skin is frozen and a hole the size of a nickel is drilled in the skull.

AIMING ARC controls angle of entry

3. Dura is opened, blood vessels are cauterized and an electrode is inserted

Surgeons begin listening for the right neurons about 10 mm above the target point

CANNULA inserted 8.5 cm deep

4. Neurons fire at different rates and patterns depending on their function. An oscilloscope reading and patient feedback confirm surgeons have hit the right spot.

Lead

Thin, insulated, coiled wires are attached to electrodes, each of which have four points of 'contact' that emit electrical current deep inside the brain to Brodmann Area 25 neurons, which, in the case of depression, are overactive

Extension

An insulated wire connects the lead to the pulse neurostimulator

Neurostimulator

The electrodes are connected by wires to a type of pacemaker device implanted under the skin of the chest below the collarbone. The device sends continuous electrical pulses to the target areas in the brain and can be easily programmed by a doctor by remote control. The dosage of the electrical impulses is customized to the individual.

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