

Deep-Brain Stimulation: Decade of Surgical Relief, Not Just for PD

21 May 2010. Twelve years on, Jeff Ryan still recalls the collective gasp in the operating room the day he got the electrodes implanted. He himself was in somewhat of a state of shock as he held the cup. “All of the sudden your hands that have been shaking like crazy all your life, are just rock steady,” he recalled. The Iowan had had essential tremor since his teens, and was starting to have trouble managing his farm because of the trembling. Surgeons ran wires into his brain and hooked them up to a pacemaker-like neurostimulator implanted in his chest, which sends electrical signals to his brain that quiet the tremors. “It just changes your life dramatically,” Ryan told ARF.

It’s not just Ryan, and it’s not just tremor. On April 28 in the *Lancet Neurology* online, researchers from Queen Elizabeth Hospital in Birmingham, UK, report on behalf of the PD SURG Collaborative Group that deep-brain stimulation plus medication led to greater improvement in Parkinson disease symptoms than meds alone. This was a six-year, 13-center trial, the largest to date ([Williams et al., 2010](#)).

In this series, ARF takes stock of deep-brain stimulation after more than a decade of life-altering procedures. Now is an interesting time to learn more about this surgical treatment, because even as scientists are gathering long-term, broad-based data on its initial indications—movement disorders—they are beginning to explore whether DBS might also work for a range of other conditions, including Alzheimer’s.

Deep-brain stimulation (DBS for short) has been used to treat essential tremor and Parkinson disease tremors since 1997, when the FDA approved the therapy. More than 55,000 DBS devices have been implanted worldwide, many targeting the tremors and dyskinesias of Parkinson disease. Doctors say even more people could benefit from DBS. “It is underutilized, in my opinion,” said Jerrold Vitek, a movement disorder neurologist and leading DBS researcher, who co-chaired the Center for Neurological Restoration at the Cleveland Clinic until his present move to the University of Minnesota in Minneapolis-St. Paul.

Scientists are starting to gather data on the long-term effects of the treatment, on symptoms as well as quality of life. In the case of Parkinson’s, the effects of DBS can seem miraculous—but it is not a solution for all life’s ills, recipients and researchers find. Sometimes, once the tremors and dyskinesias have stopped, problems can arise in other aspects of a person’s life such as work or relationships (see [Part 2](#) of this series).

Beyond PD, clinical trials are running for myriad targets. The specific site for DBS is based on imaging studies showing where, in a given condition, the brain is struggling. Therefore, any condition linked to altered brain activity in a particular spot is a potential candidate for DBS (see [Part 3](#) of this series). Neurosurgeons implant tiny wires, usually carrying four electrodes each, into the appropriate brain area. In a second procedure, surgeons place a neurostimulator just beneath the skin, frequently below the collarbone. Wires under the skin connect the two implements. The neurostimulator can provide electrical signals that are strong or weak, fast or slow, depending on the person’s needs. Researchers hope to improve both the surgical

process of DBS—making it safer—as well as the post-operative process of programming the neurostimulator to provide the ideal signals (see [Part 4](#)).



In deep-brain stimulation, a neurostimulator under the skin drives current to electrodes implanted into the brain. *Image credit: St. Jude Medical*

Optimizing Outcomes

In the most recent study of DBS outcomes, the Birmingham researchers and colleagues throughout the UK followed 366 people with advanced Parkinson disease ([Williams et al., 2010](#)). Half received DBS plus the best medical therapy available; the other half received only medical treatment. One year on, people who had surgery reported better mobility, ease in daily activities, and a drop in discomfort. People on the best medical therapy, in comparison, reported little change in their condition.

However, the scientists noted, DBS also led to more serious side effects, including 16 people who contracted infections at the surgery site, and one who died during the procedure. Because of the risks, the authors recommend that surgeons carefully select the people who are most likely to benefit from DBS.

Not everyone with Parkinson's is a good candidate for DBS. Recipients must have had a PD diagnosis for at least five years to ensure they really have Parkinson's. (Diagnostic accuracy for PD is low.) Surgeons generally restrict the treatment to people younger than 70, who they reason are best able to handle the risks of brain surgery and most likely to benefit from the chance to lead a more physically active life, said Elena Moro of Toronto Western Hospital in Ontario.

The people who respond best to surgery are those who already respond well to medication. Those people turn to DBS because the medication, after some years, often begins to cause uncomfortable side effects, such as the involuntary movements of dyskinesia, or because the medication wears off too quickly. For people who have taken PD meds such as levodopa for several years, life is a continuous cycle of “on” time, in which the drugs control symptoms well, and “off” time, when the medication wears off and they find themselves slow, trembling, even frozen in mid-movement. Peter and Barbara Higgs, both retired teachers in Workworth, Ontario, recall planning their outings and travels around the “on/off” cycle of Peter, who has Parkinson’s. Now “on” much of the time with his stimulator, Peter walked the 5K Parkinson SuperWalk in Peterborough, Ontario, last year. On average, people with DBS gain more than four hours of “on” time each day (see [ARF related news story](#) on [Weaver et al., 2009](#)).

However, people who do not find levodopa helpful may actually have a condition different from the “standard” Parkinson’s, such as dementia with Lewy bodies (DLB) or progressive supranuclear palsy, and the surgery is unlikely to help them. Some 15 percent of people with Parkinson’s meet the eligibility requirements for DBS, according to Moro.

Long follow-up studies show that even after five years—the maximum time yet published—DBS continues to support mobility. Among five people in a recent study of DBS recipients, subjects had nearly 60 percent less motor trouble while “off” medication than they did before the operation five years earlier. And the average dose of levodopa these people were taking dropped by half ([Zabek et al., 2010](#)). In another study of 49 people, researchers found similar improvements, although they also recorded some worsening of symptoms between the first and fifth year post-surgery ([Krack et al., 2003](#)). However, the authors noted that is to be expected from a progressive disease such as Parkinson’s.

Mysterious Ways

These outcomes are fairly impressive for a treatment that neither doctors nor scientists truly understand. DBS has its roots in chronic pain and tremor treatments of the 1970s, in which surgeons would simply destroy the area they thought was causing the problem. During the 1980s and 1990s, doctors found they could get similar effects by stimulating the area, a reversible treatment ([Benabid et al., 1987](#); [Benabid et al., 1991](#)). “Maybe we excite cells with the high frequency, or maybe we change the pattern of discharge of these neurons, making them more normal,” Moro said. “Nobody really knows.”

Researchers also remain uncertain which brain region is the ideal target for Parkinson disease. In the majority of DBS operations, surgeons implant electrodes into the subthalamic nucleus (STN). This area is part of a circuit that connects dopamine production in the substantia nigra, commonly reduced in PD, to movement. Another part of this circuit is the globus pallidus internal segment (GPi), which also occasionally finds itself targeted by DBS. Each has its merits. The STN is easier to find in the brain and smaller, making it easier to place the electrode exactly where it belongs. But some scientists think that GPi stimulation minimizes side effects ([Okun et al., 2009](#)). Researchers are currently comparing the two regions directly in [clinical studies](#).

The motor circuit that contains both the STN and GPi also feeds into non-motor functions. Therefore, DBS can have unintended consequences. Most side effects are mild; they include tingling in the limbs, slight paralysis, slurred speech, and loss of balance. They are often transient, occurring just after the stimulation turns on, or can be controlled by reducing the voltage delivered to the brain electrodes. Speech problems are of special concern, since some people with Parkinson's already struggle to speak at a steady volume and enunciate words clearly. In a survey of 249 people with Parkinson's, 99 of whom had had DBS, the nonprofit Parkinson Alliance found that speech dysfunction was a problem in both groups, but more so in the DBS subjects ([Parkinson Alliance, 2009](#) [.pdf]).

Cognitive function and sleep are also areas of current interest, Moro said. In another Parkinson Alliance survey of 87 people with DBS and 76 without, the group found that people with DBS reported longer and less disturbed sleep ([Parkinson Alliance, 2007](#) [.pdf]). As far as cognition is concerned, some DBS recipients show slightly reduced verbal fluency and vocabulary, working memory, and processing speed ([Williams et al., 2010](#); [Weaver et al., 2009](#)). However, Moro said, these are decrements that come up on specific neuropsychological tests, and are unlikely to cause problems in a person's day-to-day life.

"For a lot of people, it is just the simple everyday things that make the most difference," Ryan said. Successful DBS could mean regaining the ability to shave, hold a glass full up to the brim, or toss a baseball to a child. Or even simply to express emotion, Peter Higgs said: "I can smile again."—Amber Dance.

Deep-Brain Stimulation: Steadies the Body, But What About the Mind?

24 May 2010. With a few electrodes deftly threaded into a troubled brain, surgeons can often still the embarrassing tremors and alleviate the painful muscle cramps that come with Parkinson disease. But this deep-brain stimulation does not treat all that Parkinson's does to a person. People may still have to cope with declining cognitive abilities, speech difficulties, or poor impulse control. And although DBS can quell some symptoms, it does not halt the inexorable progression of neurodegenerative disease. Sometimes, aspects of a person's life—success at work, or in personal relationships—suffer following the huge upheaval that successful DBS surgery tends to bring with it. DBS can even break up a marriage.

Despite doctors' best efforts, some people have unrealistic expectations for their outcomes, said Elena Moro of Toronto Western Hospital in Ontario. Unfortunately, the surgery's results are not a sure thing, and people's hopes are sometimes dashed. "It's not working for me," wrote J.R. Jay, a retired woman in Mobile, Alabama, in an e-mail to ARF. "I can't tell you how I feel." Jay had DBS for essential tremor. She has now been told the malfunctioning equipment necessitates a second surgery, but is seeking a second opinion. "I'm not happy," she wrote.

Less Than a Miracle

People go through many changes following DBS, some positive, and some negative. In a [survey](#) [.pdf] conducted by the nonprofit [Parkinson Alliance](#), people who had

DBS reported less anxiety than those whose Parkinson's was managed by medication alone. However, reports of depression were no different between the groups.

Some aspects of disease may remain the same, or even worsen, with deep-brain stimulation. For example, DBS can adversely affect speech, already a problem in people with PD—although in at least one case, DBS relieved stuttering in a person with PD ([Walker et al., 2009](#)). Impulsive behavior, such as hypersexuality or addiction to gambling, may remain after DBS or even worsen. In one instance, scientists in Amsterdam, The Netherlands, reported on a man who got hooked on slot machines after his DBS surgery. He had no history of compulsive gambling; indeed, family members described him as “stingy.” Dopamine agonists can also influence impulsive behavior, so his doctors were eventually able to control the compulsion by altering his medication ([Smeding et al., 2007](#)).

Emotional responses, too, may be altered by DBS. In a recent Danish study comprising in-depth interviews with people before and after DBS, one person told the researchers, “I have become much more sensitive; I cry over nothing” ([Voon et al., 2008](#)). Another research group found that following DBS, many people with Parkinson's are less able to recognize the emotion in other people's faces—particularly fear and sadness ([Péron et al., 2010](#)).

The potential side effects worried Greg Rice, a retired banker in Dover, Massachusetts, who had DBS for Parkinson's five years ago. Rice has had Parkinson's since 1993. Before his surgery, he had developed a late-blooming musical streak, [composing symphonies](#). He suspected that his disease, plus a divorce in the late 1990s, unleashed his creativity, and with Parkinson's keeping him from sleeping, he spent many night hours composing. He initially feared DBS would give him back mobility but take away this creativity. However, when he reached a point where he fell down 30 times a day, Rice decided the risk was worth taking.

Post-op, Rice is happy to still be composing, with the added benefit that he no longer falls down so often. Most importantly, he told ARF, the involuntary dyskinesia has stopped. “I would do it again even if I did lose the creativity, because the dyskinesia was driving me crazy,” Rice said. However, the surgery did not solve everything; he still struggles to speak intelligibly and sometimes gets “frozen,” crashing into things when he unfreezes. He copes with his disease by focusing on what he can do for others, working with his church, and coaching his daughter's softball team. He was careful to note that DBS is not for everyone.

New Body, New Life

Symptomatic improvement in one arena does not always translate to the rest of a person's life. For example, in a study of 23 people, researchers in Houston, Texas, found that people generally experienced greater energy levels and needed less help from a carer following DBS. But at the same time, the researchers found, some DBS recipients were unable or unwilling to apply their newfound abilities to succeed in the workplace, maintain interpersonal relationships, or to do more fun activities ([Ferrara et al., 2010](#)).

Researchers in France, who conducted pre- and post-op interviews with 29 DBS recipients, found similar results. In fact, they wrote, “Marital life and professional

activity...worsened more often than they improved.” Of 16 participants who were working before surgery, only nine returned to work afterward. Social lives generally improved, but some participants reported that although they now had the physical ability to go out, they had no friends to see ([Schüpbach et al., 2006](#)).

The French study included 12 couples that had no notable marital problems before the surgery. In five of those couples, conflict arose post-operatively. It turned out that surgery changed a caregiver-patient dynamic that many couples were used to. In the study, the researchers noted one woman who spoke of her husband’s surgery: “When he was sick, we were a perfect couple. Now he wants to live the life of a young man, go out, meet new people; all of that is intolerable! I would rather he be like he was before, nice and docile!”

Families tend to stick together when someone is sick, said Helen Mayberg of Emory University in Atlanta, who was not involved in the study. But once a partner is physically independent, some caregivers may no longer feel obligated to stay in the relationship. Alternatively, people who previously needed care may want out of a relationship, and DBS gives them the opportunity to leave. Anthony Lang, a leading Parkinson’s physician-researcher at the Toronto Western Research Institute, noted in a plenary lecture at the 2009 AD/PD conference in Prague, Czech Republic, that response to DBS has become one of the more common reasons for divorce among PD patients. This has prompted some discussion among experts on whether the surgery should be offered at earlier stages of disease to people who are still more active and better able to make the most of their motor improvement without upending their pre-op life.

Any major surgery can cause upheaval, and for some people, the change is too much to bear. Researchers in a 55-center, global survey of more than 5,000 people who had DBS for Parkinson’s found the overall rate of successful suicide was 0.45 percent, and the attempt rate was 0.90 percent. When they compared post-DBS rates to the general population suicide rates in each country in the study, they found that DBS increased the suicide risk. The increased suicide rates continued for at least four years following the operation ([Voon et al., 2008](#)). Both researchers and patients suggest that a DBS team should include not only physicians and neurologists, but also psychologists or psychiatrists to guide people through the transition.

And in most cases, it is a transition worth making. For example, retired teachers Barbara and Peter Higgs, of Workworth, Ontario, were thrilled with the results of Peter’s DBS for Parkinson’s. “I am not that keen on being a caretaker, to tell you the truth,” Barbara Higgs said. “I was delighted to see him regain control of his life.” And the French study authors noted that despite mixed results from their surgery, none of the 29 people in their study wanted to turn the device off.—Amber Dance.

Deep-Brain Stimulation: An Electrode for All Occasions?

25 May, 2010. Deep-brain stimulation (DBS) is not just for shakes and trembles any more. With the advent of improved brain imaging, researchers are linking certain parts of brain anatomy to conditions ranging from addiction to Alzheimer disease.

And for every MRI or CT scan showing a hot spot, it seems, there increasingly is a surgeon waiting to stick an electrode in it. “I do not think there is any disease that is ‘safe’ right now,” quipped Jerrold Vitek, a dementia with Lewy bodies (DLB) pioneer who is set to take over the Department of Neurology at the University of Minnesota in Minneapolis-St. Paul this July. “If you have a hammer, everything looks like a nail.”

DBS is creeping into the realm of psychiatric disorders such as obsessive-compulsive disorder (OCD), Tourette syndrome, and depression. Small studies show that the treatment is often effective and causes minimal side effects (reviewed in [Kuhn et al., 2010](#)). In part, the use of DBS in psychiatric conditions was inspired by unexpected results when doctors attempted stimulation to treat Parkinson’s. A couple of people with both PD and OCD, who received DBS for the Parkinson’s symptoms, also experienced a reduction in obsessive and compulsive behaviors ([Mallet et al., 2002](#)). In another case, a woman who received DBS to relieve Parkinson’s experienced profound sadness when certain parts of her brain were stimulated. The effect quickly disappeared when the electrodes were turned off ([Bejjani et al., 1999](#)). These side effects led researchers to suspect that thoughts and feelings, as well as movement, could be subject to alteration by DBS. Conditions such as Tourette’s (reviewed in [Temel and Visser-Vandewalle, 2004](#)) and OCD ([Jung et al., 2006](#)) have also responded to deep brain lesions, a precursor to DBS used in the past.

Diminishing Depression

Given the small but real risks inherent in brain surgery, DBS tends to become an option when a disease is serious and other therapies have failed. There are many conditions that, at least in some people, resist the best medicine currently on offer. For example, Helen Mayberg of Emory University in Atlanta, Georgia, works on treatment-resistant depression (TRD). The patients she works with have had major depression for years, and tried medication, psychological therapy, and electroconvulsive therapy, to no avail. Many are unable to work. “They are dangerously and intractably ill,” she said.

Mayberg was able to turn the images she saw on brain scans of sad or depressed people into a novel therapy for the condition. This is the first time, Mayberg said, that a targeted treatment came directly from images, with no other basis for potential efficacy. She and others observed that the subgenual cingulate cortex is overactive in people with TRD. Activity in the region also turns up with negative mood in healthy people ([Mayberg et al., 1999](#)). “We are interested in turning the activity down,” Mayberg said.

Mayberg, then at the University of Toronto in Ontario, initially tried DBS of the subgenual cingulate in six people ([Mayberg et al., 2005](#)). Later, she and others expanded the trial to include 14 more patients ([Lozano et al., 2008](#)). They saw effects even in the operating room, when surgeons stimulated the target area to make sure electrodes were properly placed. Spontaneously, some subjects reported that the room suddenly looked brighter, or that they experienced a “disappearance of the void” ([Mayberg et al., 2005](#)). By six months after the surgery, 60 percent of recipients had some response, and 35 percent were considered in remission ([Lozano et al., 2008](#)). DBS for depression is currently under trial in a study run by St. Jude Medical, Inc., of St. Paul, Minnesota, a maker of DBS devices, Mayberg said.

Mayberg cautioned that DBS marks only the beginning of a person's recovery from TRD. "This does not make you happy," she said. "This turns negative off." The recipient must take the next step to regain a positive outlook. And just as a person who has, say, hip replacement surgery needs rehab, people who have DBS for depression need "psychological rehab," Mayberg said, to help them adjust.

If I Had a Hammer....

Currently, DBS is FDA-approved for essential tremor, Parkinson disease, and dystonia. The FDA also allows some people with OCD to receive the device. Efficacy for this condition is [under study](#) but remains unproven. Beyond that, researchers are trying DBS for a whole laundry list of conditions (reviewed in [Awan et al., 2009](#)). Clinical trials are underway for [Huntington disease](#), [cluster headache](#), [pain](#), [epilepsy](#), and [Tourette syndrome](#).

Some scientists hope that even conditions that cause their primary pathology outside of the brain may respond to DBS. For example, amyotrophic lateral sclerosis manifests primarily in the spinal cord—but researchers using single-photon emission computed tomography discovered lesions in the cortex of four people with ALS. They attempted DBS with these four in a preliminary study. Two years later, two of the people had only mild progression of the illness, which is normally fatal within three to five years, and their lesions had disappeared. The third recipient's disease continued to progress after the first few months; the fourth, however, committed suicide ([Sidoti and Agrillo, 2006](#)).

Most DBS targets are based on what researchers know about how the brain works, but at least one, for Alzheimer disease, was discovered by more roundabout means. In 2008, researchers from Toronto Western Hospital in Ontario reported on a surprising finding ([Hamani et al., 2008](#)). They were hoping to help an obese man stem his desire for food. The 50-year-old, 420-pound man had tried dieting, psychological therapy, and medication without success. He feared that even if he received bariatric surgery, he would continue to overeat.

The researchers targeted the hypothalamus, an area known to influence feeding in animals ([Takaki et al., 1992](#)). In the past, doctors had targeted this region with lesions to treat obesity ([Quaade, 1974](#)).

During the surgery, the doctors turned on the signal to the electrodes to ensure they were hitting the target area. They asked the man, who was awake during the procedure, if he felt any change in hunger. He did not—but he did notice a strange sense of déjà vu. Suddenly, he flashed back 30 years to a scene in a park, surrounded by friends. He recognized his girlfriend from that time. When the doctors turned off the stimulation, the memory vanished; they turned it back on and the memory resurfaced.

"We were caught completely by surprise," said study author Andres Lozano. "We knew immediately that this was something very significant."

The hypothalamus is involved in memory as well as appetite ([Soriano-Mas et al., 2005](#)). In tests following the surgery, the researchers also found the obese man was more likely to remember word pairings when the stimulator was on; using

electromagnetic tomography, they saw that the stimulation activated the brain's memory circuit. (They used this method because the man was too large for a standard PET or MRI scan.) As to the effect on obesity, the man reported reduced cravings and did lose more than 25 pounds, but gained them back when he started turning off the neurostimulator to snack at night.

Based on this serendipitous, if anecdotal, finding, the researchers launched a [small trial](#) with six subjects to see if DBS can improve memory in six people with mild Alzheimer disease. Although DBS cannot repair the degenerated tissue lost in Alzheimer's, Lozano hopes that it can improve input to "innocent bystander" parts of the brain that, while healthy themselves, are missing input from damaged neurons. Lozano expects to publish the results within the next few months. Researchers in the French city of Nice in 2009 listed a [similar trial](#), though it is not recruiting yet.

In a related study, researchers in Germany this year began testing [DBS for Alzheimer's](#). Unlike the Toronto and the Nice groups, who are targeting the fornix region, this group is tickling the nucleus basalis of Meynert, an area known to degenerate in AD (see [ARF related news story](#) on [Freund et al., 2009](#)).

"These are exciting times," Mayberg said of the rapidly expanding DBS field. "As we learn more about the brain, we are going to be able to help people in ways we had not thought about before."—Amber Dance.

Deep-Brain Stimulation: There's Still Room for Improvement

26 May 2010. Though some 55,000 people have received deep-brain stimulation for conditions ranging from Parkinson disease to obsessive-compulsive disorder, there is still plenty of room to improve the process. Companies are working on smaller devices with longer battery life. Surgeons are seeking ways to more safely and precisely implant the electrodes that reset faulty brain signals. And people who receive DBS are hoping that researchers can improve the sometimes lengthy and cumbersome process of fine-tuning the settings on the pacemaker-like neurostimulator that controls the pulses to the electrodes.

Ever-improving imaging technology has been key to the spread of DBS, as doctors identify more brain regions that might benefit from the stimulation. For example, researchers have gone as high as seven-Tesla MR imaging, in comparison to the standard two Tesla scanners more routinely available ([Cho et al., 2010](#)). These high-resolution images help surgeons target the right spot. "Getting the electrodes in the right place is probably the most important thing to dictate clinical outcomes," said Cameron McIntyre of the Cleveland Clinic. A millimeter to the left or right, and results will be less impressive than they could be. And this placement happens some six centimeters below the skull, where surgeons cannot navigate by sight.

In the OR

To help surgeons turn the images from an MRI or CT scan into a plan of operation, McIntyre and others have developed a software package called Cicerone ([Miocinovic et al., 2007](#)). The software lines up a person's brain scans with standard

neurophysiology maps and 3D brain atlases, so surgeons can identify the most promising site for stimulation and plan a route to get there. During the operation itself, the surgeon can also use the images to visualize the electrode's location, and Cicerone will predict what regions it will stimulate.

In addition to placing the electrode, better images help doctors plan a safe surgery. The location of blood vessels varies from person to person, and surgeons may nick one, causing a hemorrhage. The risk of serious bleeding, leading to brain damage or death, is between 1 and 2 percent. Neurologist Jerrold Vitek, soon to move from Ohio's Cleveland Clinic to the University of Minnesota in Minneapolis-St. Paul, said he wants to see that risk drop to 0.5 percent, so more people who might benefit from DBS will feel confident signing up for the procedure.

A person who receives DBS will likely need brain surgery once, but will also have a second surgery to implant the neurostimulator in the chest. It connects to the brain via wires under the neck's skin. That surgery is necessary every time the neurostimulator's batteries run out and require replacement—once every two to five years, depending on the voltage settings.

But Richard McEnery, a software developer and photographer in Sammamish, Washington, was burning through batteries in a year, he told ARF. DBS silenced much of his dystonia—a condition that includes involuntary muscle contraction—including the neck tremors that made him “look like a bobblehead doll,” he said. Now, McEnery benefits from a relatively new improvement in DBS technology, a rechargeable battery. It doesn't last as long—perhaps a month—but he can top it off at home while watching TV. The recharger is a large plastic device connected to a battery. Once a week, McEnery dons a harness that aligns the recharger with the neurostimulator under his skin. Over an hour or two, the device wirelessly transmits power through his skin to the neurostimulator, and he is powered up and good to go.

Post-Op

DBS is not plug-and-play; the equipment requires setting and maintenance. Neurostimulator settings include many parameters; voltage, signal length, and frequency of stimulation are just a few. A doctor or nurse works with the DBS recipient to program the neurostimulator's activity. Altogether, thousands of possible setting combinations exist, and every recipient needs a personalized one. Finding those magic numbers requires multiple office visits that can last hours. The time involved—and lack of many healthcare practitioners skilled in setting the device—is one of the biggest complaints among people who have DBS. McEnery recalls it took a year to perfect his settings.

The programming task frequently falls to nurses, neurophysiologists, and doctors still in training, who may or may not be expert in the process and in medical treatments for the condition at hand. In a 2006 study, researchers at Toronto Western Hospital examined the potential for an experienced neurologist to improve programming ([Moro et al., 2006](#)). They initiated the study when Elena Moro, an expert in DBS as well as management of Parkinson's and movement disorders, joined the clinic. She reset neurostimulators for 44 people with Parkinson's who had had DBS for an average of 3.5 years already. The result: more than half of the participants saw improvement in mobility and daily activities, and were able to reduce their anti-

Parkinson's medications. Others saw no benefit; in four people, symptoms worsened. The data suggest, the authors write, that the expertise of the programmer makes a difference.

"A great deal of clinical intuition goes into the process," said McIntyre, who was not involved with the Toronto study. Yet again, he offers a computational solution. He and colleagues are developing StimExplorer, a program that integrates a patient's MR images with the position of the electrode ([Butson et al., 2007](#)). It offers users a set of theoretically optimal parameter settings. They may not be just right, but they should, hopefully, put the user in the right ballpark from which fine-tuning is easier. McIntyre has licensed much of his technology for commercial development, and hopes his software will receive FDA approval in a year or two. Something like StimExplorer could help inexperienced programmers, Moro said.

As DBS becomes more popular, more companies are developing stimulators. Medtronic, Inc., headquartered in Minneapolis, Minnesota, currently holds much of the U.S. market. St. Jude Medical, Inc., based in St. Paul in the same state, already has a DBS device approved for Parkinson's in Europe and is currently conducting a U.S. study. Competition should lead to improvements in the technology. For example, doctors hope to soon have a neurostimulator small enough to fit in the head, against the skull. This would eliminate the wires traveling through the neck, which might break. "I think you will see a lot of one-upmanship between the two players," McIntyre said.—Amber Dance.