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TECHNOLOGY

Monitoring gets personal

By bootstrapping existing technologies, researchers can gain a minute-by-minute understanding of a patient's disease.

BY LAUREN GRAVITZ

When Steven DeMello started his job as a health-technology researcher, he had no idea that he would soon become a participant in his own research. As part of a University of California initiative, he spent his days studying the potential uses of communication technologies, such as smartphones, in health care. But just a few months into the job, he was diagnosed with Parkinson's disease. One month later, he was told he also had cancer.

He was surprised by the difference in care between the two diseases. To monitor his particular cancer, a rare form of lymphoma, he has a regular blood test, which was weekly at first. Five objectively measured markers tell DeMello and his oncologist what is going on. "When we sit down and look at results over time, we have consistent testing," says DeMello. "We know the values matter, and we know why they matter."

With his Parkinson's, however, there is no unbiased, quantitative way to assess disease progression. Every four months or so he visits his neurologist, who runs him through an assessment to determine where he falls on the unified Parkinson's disease rating scale (UPDRS) — a universal test created, used and validated by neurologists worldwide. He reports any changes in mood, cognition or physical abilities, and he is assessed for tremor, rigidity and irregularities in his gait. The UPDRS test is invaluable, and has been improved over the years, but it is labour intensive. It must be administered by a neurologist, and its results are subjective and depend on how patients such as DeMello are doing at that particular moment — something that, for someone with Parkinson's, can vary hugely from hour to hour, let alone day to day.

There is nothing inherently wrong with the contrast in care, which reflects the different characteristics of these diseases. Cancer can attack rapidly, requiring aggressive treatment, whereas Parkinson's is a chronic disease that might have daily ups and downs but in general progresses over decades. Yet there is much to gain from frequent and quantified monitoring of Parkinson's disease, and many physicians, patients and their carers are keen to have a reliable way to do so.

DeMello knew of a new technology that might help. He downloaded an experimental smartphone application called mPower. "I used what I've learned about mobile applications with myself as a guinea pig," he says. The iPhone app administers a few simple tests — getting him to tap the screen, hold the phone in an outstretched arm or put it in his pocket and walk across the room — so that he can objectively measure and keep tabs on his symptoms on a daily basis.

In the past decade, as smartphones, smartwatches and exercise trackers have become more pervasive, the sensors they carry have got more advanced. These are tantalizing tools for researchers looking to monitor everyday movements. And because Parkinson's is a progressive disorder that affects a person's motor skills, it is a good candidate to test the sensors. Scientists are tapping into this technology to gain a more granular look at the symptoms and progression of this insidious disease.

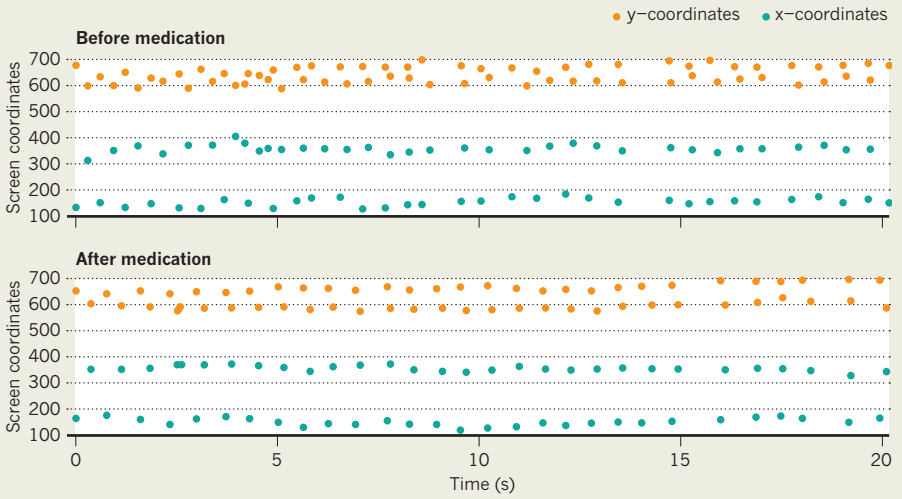
GROWING POTENTIAL

One of the researchers who helped to develop the mPower app is Max Little, a mathematician at Aston University in Birmingham, UK. Little broke ground in the remote assessment of Parkinson's back in 2006, when technology company Intel recruited him for a project. Intel had amassed thousands of voice recordings from people with the disease, and — because Little had recently developed an algorithm that could identify voice disorders — it was interested in whether he could use the recordings to

LEFT, ANDONG ZHAN; RIGHT, MAX LITTLE & ANDONG ZHAN

SMART DATA

The touch screen of smartphones can help to evaluate motor function remotely by monitoring finger tapping and reaction times. The graphs show that tapping coordinates (top) are more consistent after taking medication (bottom).



distinguish people with Parkinson's from those without. Little's algorithms were so successful at identifying people with the disease that he began to look for other opportunities to use them for remote monitoring. When he began a fellowship in a lab that specialized in human–smartphone interactions (and how those data can objectively quantify behaviour), the pieces clicked into place. He has been working on ways to use smartphones to monitor Parkinson's ever since.

"Smartphones are pretty miraculous things that are packed full of sensors," says Little. "We're walking around with devices that measure movement and hence behaviour all the time." Little is investigating approaches that use these sensors to assess the disease. The microphone records someone's voice; a triaxial accelerometer detects their movement in three dimensions to provide information on gait, posture and hand tremor; a gyroscope measures rotation; and the touch screen can evaluate finger tapping and reaction time.

"Smartphones are pretty miraculous things that are packed full of sensors."

Such information might reveal whether a new therapy is effective, an old therapy remains effective, or whether it might be time to change the dose or medication. "I've been using mPower as a way of trying to understand my own trends and, in particular, my own variability," says DeMello. The app provides a long-term view, so that when he has a few bad days in a row, he is no longer concerned. "That's something that, a few years ago, I would have been much more worried about," he says. The data show him that, at this point in his disease, a run of bad days will turn around. "It's giving me a way to understand my own patterns."

Despite its obvious allure, tapping into technology that people already have in their pockets is no simple solution for detecting medically important events. mPower was developed to collect a huge amount of data, which researchers could sift through to work out which pieces are useful — just as Little did with the voice recordings. But it is difficult to mine vast amounts of data when there is no certainty that something significant will show up, says Joe Giuffrida, president of Great Lakes NeuroTechnologies, in Cleveland, Ohio.

Giuffrida's company has developed wearable, sensor-packed devices and apps that are dedicated to tracking the symptoms of Parkinson's. Rather than trying to pick out a signal from a sea of unverified data, Giuffrida says that it makes more sense to know what you're looking for before starting the analysis. "To develop algorithms, you need gold-standard data to test their output," he says. "When you just put sensors on a patient and let them loose in the world, it's hard to have that gold standard." Great Lakes put its sensors on people with Parkinson's disease and gathered data while neurologists determined the participants' UPDRS scores. Then the company recorded thousands of hours of video of the participants wearing the sensors. This allowed its researchers to identify specific moments in the video and sensor data that correlated with different UPDRS scores, and build algorithms using these known quantities.

The Great Lakes approach is time- and cost-intensive, however, and the company will charge for the wearable sensors and for a monthly subscription to the app. mPower is free, but before people can use it they must consent to trial conditions and allow their data to be sent back for analysis. And those data are constantly assessed. Andong Zhan, a computer-science PhD candidate at Johns Hopkins University in Baltimore, Maryland, helped to develop an app for the Android platform that was an early prototype for mPower. The Hopkins-PD app is also being assessed in several trials, including one called Smartphone-PD, which has been running since 2014. Zhan says that the trial has finally gathered enough data to start verifying the algorithms. The researchers are collaborating with Ray Dorsey, a neurologist at the University of Rochester Medical Center in New York, who is assessing some of the people with Parkinson's across the state by teleconference before the patients test themselves using Hopkins-PD. "He gives them a score, and then we correlate that with our score from the smartphones," Zhan says.

Using a general device, rather than one that is specifically made for monitoring, can create issues with data quality. "Because the tests are done at home using smartphones, some of the data can be very noisy," says Siddharth Arora, an applied mathematician also at Aston University, who is also working on Hopkins-PD, with a focus on data quality. "In a lab, we can control for confounding factors." The home environment is much less predictable. For a voice test, for instance, there might be someone coughing in the background, he says.

Nevertheless, the Hopkins-PD algorithm is producing some striking preliminary results. The results for a finger-tapping test, which assesses a person's motor function, indicate noticeable improvement for some participants after they have taken their medication (see 'Smart data'). The app also records more nuanced information. "It's so exciting to see that simple software and hardware could pick out subtle differences in motor performance in people with Parkinson's," he says. For now, Arora, Little and their colleagues are honing the app. And others — including drug and medical-device companies — are actively involved in similar experiments.

TESTING TIMES

Smartphone apps may also allow for a change in how Parkinson's therapies are tested and approved. Little is collaborating with the pharmaceutical division of Roche, based in Basel, Switzerland, which has developed a smartphone app for use in a Parkinson's trial.

One problem with drug trials is that the

participants, just like other people with Parkinson's, are assessed only a few times a year. With such sparse data collection, as DeMello discovered, it is difficult to quantify someone's symptoms and disease progression, let alone gain any detail about how a drug affects them under real-world conditions. What's more, assessments can be affected by the disposition of everyone involved on that particular day. "They're highly subjective," says Christian Gossens, who heads the early development informatics team at Roche. Technology is free of such whims. The app, Gossens notes, "takes away all influence of mood or stress" for both the patient and the physician, and eliminates differences between observing physicians.

The app is being informally assessed as part of a current trial, and the Roche researchers are already seeing benefits. "If you want to zoom into an individual patient, and zoom into disease progression a certain way, now you can," Gossens says. When you look at a group of patients, or general properties of a disease, he says, "things look like they're on a continuum. But the more you zoom in, the more they become discrete." Such granularity allows researchers to find and analyse more specific aspects of both drugs and disease.

If the app proves useful, Roche will consider including it in future trials in order to file for US Food and Drug Administration (FDA) approval. For now, the FDA remains curious, Gossens says. It wants to know what is technically possible, how it could be valuable, and how future trials of such an app could be regulated.

Bootstrapping existing technologies and using them in ways for which they were not intended can yield game-changing results. There are no biomarkers for Parkinson's that definitively identify the disease in its earliest stages. But Little says that he and his colleagues have preliminary evidence that the same smartphone tools can detect sleep issues, which are emerging as useful early warning signs for Parkinson's (see page S5).

And then there are applications in countries with less-developed health-care infrastructure. "More than 2 million Parkinson's patients haven't been diagnosed in China," Zhan says. "Some don't know they have it, and some can't access good health-care resources for diagnosis or treatment." Zhan imagines a day when a smartphone app could be used in countries such as China and India as an inexpensive, simple way to monitor people who have the disease — or even to help with diagnosis.

Smartphones have huge potential, Little says. "We're really only beginning to scratch the surface of what it's possible to do with this technology." ■

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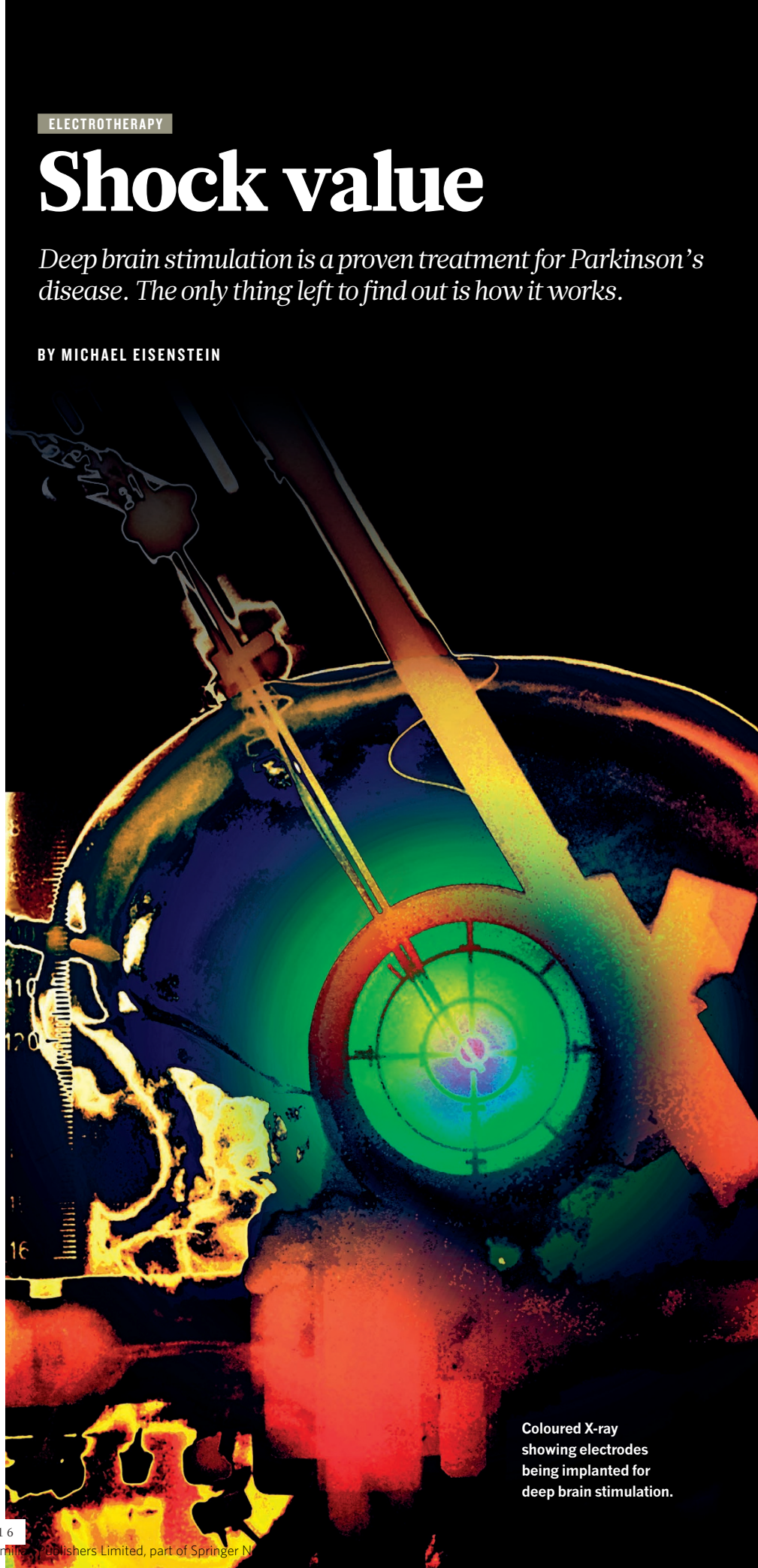
ELECTROTHERAPY

Shock value

Deep brain stimulation is a proven treatment for Parkinson's disease. The only thing left to find out is how it works.

BY MICHAEL EISENSTEIN



Coloured X-ray showing electrodes being implanted for deep brain stimulation.