



Unlocking the secrets of the brain's connection to pain

Advanced brain imaging, led by doctors like Karen Davis, is bringing patients one step closer to personalized precision pain solutions

Judy Gerstel

Dr. Karen Davis has devoted her life to learning about something no one wants. And there's still so much to learn, she says, about pain.

She was turned on to the topic by her North York, Ont., high-school biology teacher, Marty Greenberg.

"He was excited because they'd just discovered opiate receptors," she recalls. "It was a cool idea that we have mechanisms in the brain to not only feel pain, but also to modulate pain."

"That really got me hooked on the whole topic of pain and pain control."

Now, many years later, Dr. Davis is an eminent neuroscientist and author of more than 150 published papers. Many have been cited hundreds of times by other scholars. She's a senior scientist and division head at the Krembil Research Institute and a professor in the Department of Surgery at the University of Toronto.

Her highly informative TED-Ed video entitled "How Does Your Brain Respond to Pain?" has been viewed more than 1.1 million times.

Dr. Davis still finds the work of the brain and how it relates to pain fascinating. For example, she references "making a small lesion in the brain to target a specific area of pain."

Early results of a research study of the

treatment for trigeminal neuralgia (a facial pain syndrome) were extremely promising in some patients, she reports.

"The patients who responded showed reversal of abnormalities in one part of the brain. That's [exciting that] treatment is reversing abnormality."

Innovative research in neuroscience, Dr. Davis explains, "is not only about what is not working, but also about what parts of the brain have the capacity to bring about change."

She'll be studying exactly that as one of the principal investigators of the Chronic Pain Network.

It's one of five new national research networks in a \$62.5-million federal program called Canada's Strategy for Patient-Oriented Research.

"Chronic pain is so widespread in our society," says Dr. Davis. "Studies have shown how prevalent it is. But society just wants you to grin and bear it."

One in three Canadians experiences chronic pain, and the cost for health care, wages and lost productivity is more than \$40 billion annually.

"Society tends to focus research dollars and attention on diseases that can kill you, and rightly so," she says, "but chronic pain is an enormous, silent societal issue."

Discussion about medical assistance in dying brought the issue "out of the closet," Dr. Davis says, "because pain and suffering can be so severe that people want to end their lives."

She's met many patients with chronic pain conditions who weren't believed. "They were told it's psychological, all in their head, and this influenced how their employers and family members regarded them."

But with scanning technology, she explains, "we were able to show that their brains were functioning abnormally (in response) to pain originating, for example, in the gut from IBS (irritable bowel syndrome)."

"These patients were thankful to know that it was real, that it's not a psychiatric condition, not malingering. The brain response is abnormal. There are many chronic pain conditions where patients are told they're making it up or exaggerating," Dr. Davis says.

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- Dr. Karen Davis

"But you can see on the scans that their brains are not normal."

This, says Dr. Davis, "is the first step in not only helping patients understand what's going on, but also showing physicians and the world that they need to take these patients more seriously and look at treatments that tap into abnormality."

Investigating and making known those abnormalities has motivated Dr. Davis from the beginning.

"When I started university," she recalls, "I sought out and was lucky to have opportunities to work in the labs of leading pain researchers."

One of her mentors was Dr. Jonathan Dostrovsky, now retired from the University of Toronto.

Normally, says Dr. Dostrovsky, "when students apply to do grad work with me, they don't really know what they would like to do. She was different. She already had a lot of her own ideas and a project she thought out entirely on her own, investigating the mechanism of signals in the brain linked to

migraine. It hadn't been investigated before."

He lists her strong points: "motivation, creativity, innovation, organization skills, leadership."

As part of her training, including post-doctoral work at Johns Hopkins University in Baltimore, she spent 15 years in operating rooms.

"I wanted to figure out what's going on by recording brain activity while patients were awake and could tell us what is happening," she explains.

And then a sea change happened in the field of neuroscience.

"Brain imaging came along. It was a huge leap in looking at the whole brain, including the brains of healthy people, to create a normal database."

While the availability of magnetic resonance imaging (MRI) was "a major, major advance," says Dr. Davis, "where we are going now, the next major advance is MEG (magnetoencephalography)."

MEG records magnetic fields produced by electrical currents in the brain, just as electrocardiogram (ECG) does in the heart.

"I'm confident that in my lifetime, we are going to get close to personalized and precision pain management," she says.

"We've had all these treatments for chronic pain that did a great job at helping a very small subset of patients. There's something different in these patients' brains that makes them respond to treatment while others don't. Not every treatment or drug works for everybody in same way," says Dr. Davis.

"With advanced brain imaging, we'll be able to non-invasively figure out brain circuits in people with conditions that look the same and find out why some are responsive to treatment and some are not."

Figuring out the variability to target, she explains, could reduce healthcare costs and "the agony of patients having to shop around for something that may or may not work."

People with end-of-life pain would benefit, as well as those with chronic disease pain.

Dr. Davis also insists that we shouldn't have to accept the aches and pains of aging.

"We should be able to figure out a way to live through our middle age years without aches and pains," she says. "A lot of people don't experience them. So we need to look at why some people are resilient or have a high pain threshold or respond well. They're going to give us clues."

It's very likely that some of those breakthroughs will come in Dr. Davis' lab and those of her colleagues at Krembil.

"In terms of pain research," she says, "Canadians are definitely known internationally as world leaders. We have a long history of tremendous research. Many of us are involved in a lot of international societies. We punch above our weight. It's something we should be proud of." ■

Should brain scans be used to measure pain?

Being able to scan the brain with advanced imaging technology provides huge benefits to pain researchers like Krembil Research Institute senior scientist Dr. Karen Davis, to clinicians and to patients.

But there's also a dark side to brain imaging.

For example, using it to prove that someone does or does not have pain, usually in legal and insurance cases, is an ethical issue that's of great concern to Dr. Davis and many colleagues.

She's spearheading an international effort to explore the ethics of using information from brain scans, how it should or shouldn't be used and by whom and for what purposes.

Dr. Davis cites the privacy issue, comparing brain scans to genetic screening, and she believes the information should be used solely for treatment that benefits the patient.

"Using brain scans to diagnose pain is something I'm against," she says firmly. "It's essentially like a lie detector test, mostly for legal cases. I've been fighting against that."

She says judges tell her they're dealing with this every day in court. "It's an issue in Canada," she adds. "People come to me that work for insurance companies."

"Can Brain Imaging Be a Pain-o-Meter?" was the title of her presentation last year at a Harvard Law School conference titled "How Neuroimaging Helps Law Re-Envision Pain."

Her answer to the pain-o-meter question is a clear "No!"

Says Dr. Davis: "It's not what the technology should be used for."

She says people with chronic pain are constantly being asked to prove they're in pain.

She now serves as Chair of the Special Presidential Task Force on "The Use of Brain-Based Diagnostic Tests for Chronic Pain." The task force is part of the International Association for the Study of Pain.