



# THE PAINFUL TRUTH

*Brain-scanning techniques promise to give an objective measure of whether someone is in pain, but researchers question whether they are reliable enough for the courtroom.*

BY SARA REARDON

**A**nnie is lying down when she answers the phone; she is trying to recover from a rare trip out of the house. Moving around for an extended period leaves the 56-year-old exhausted and with excruciating pain shooting up her back to her shoulders. “It’s really awful,” she says. “You never get comfortable.”

In 2011, Annie, whose name has been changed at the request of her lawyer, slipped and fell on a wet floor in a restaurant, injuring her back and head. The pain has never eased, and forced her to leave her job in retail.

Annie sued the restaurant, which has denied liability, for several

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hundred thousand dollars to cover medical bills and lost income. To bolster her case that she is in pain and not just malingering, Annie's lawyer suggested that she enlist the services of Millennium Magnetic Technologies (MMT), a Connecticut-based neuroimaging company that has a centre in Birmingham, Alabama, where Annie lives. MMT says that it can detect pain's signature using functional magnetic resonance imaging (fMRI), which measures and maps blood flow in the brain as a proxy for neural activity.

The scan is not cheap — about US\$4,500 — but Steven Levy, MMT's chief executive, says that it is a worthwhile investment: the company has had ten or so customers since it began offering the service in 2013, and all have settled out of court, he says. If the scans are admitted to Annie's trial, which is expected to take place early this year, it could establish a legal precedent in Alabama.

Most personal-injury cases settle out of court, so it is impossible to document how often brain scans for pain are being used in civil law. But the practice seems to be getting more common, at least in the United States, where health care is not covered by the government and personal-injury cases are frequent. Several companies have cropped up, and at least one university has offered the service.

The approach is based on burgeoning research that uses fMRI to understand the nature of pain — a very subjective experience. Scientists hope that the scans can provide an objective measure of that experience, and they see potential applications, such as in testing painkillers. But many neuroscientists say that the techniques are still far from being accurate enough for the courtroom. Critics say that the companies using them have not validated their tests or proved that they are impervious to deception or bias. And whereas some think the technologies will have a place in legal settings, others worry that the practice will lead to misuse of the scans.

"There's a real desire to come up with some more-objective proxy for pain," says Karen Davis, a neuroscientist at the University of Toronto in Canada. But such measures must be extremely accurate, she says. "The outcome of having a wrong answer can be quite catastrophic."

## NEURAL ORIGINS

The methods that doctors commonly use to assess pain can seem crude. People are asked to rate their pain on a scale from one to ten, or choose from a row of cartoon faces that go from happy to anguished. These measures can help to chart changes in pain, as someone recovers from surgery, for example. But each person will experience and rate their pain differently, so one person's five could be worse than another's seven, and a nine might or might not be bad enough to keep someone from working.

An objective answer should lie in the brain, where the experience of pain is ultimately constructed. And although every experience is different, pain should share some common elements. Neuroscientist Tor Wager at the University of Colorado Boulder has been trying to decipher pain's signature in the brain by placing people in an fMRI scanner while they touch a hot plate. As the researchers turn the plate's temperature up and down, they record the activity across different parts of the brain, including the sensory regions associated with the hand. From these patterns, Wager says, they can predict with better than 90% accuracy whether the plate is just warm or painfully hot<sup>1</sup>.

But this measures acute pain — the immediate response to an obvious stimulus. Chronic pain, like Annie's, affects hundreds of millions of people worldwide. And although its cause can be obvious, that is not always the case. Vania Apkarian of Northwestern University in Chicago, Illinois has scanned dozens of individuals soon after a back injury and then again over the course of a year or more. The pain went on to become chronic in roughly half of those people, and even though they described

the pain the same way throughout, Apkarian could detect a shift in the pain signature in their brains<sup>2</sup>. It changed from a signal of activity in the insula, which is associated with acute pain, to one of activity in the medial prefrontal cortex, which processes cognitive behaviour, and the amygdala, which controls emotion. "Our interpretation is that the pain is becoming more internalized," Apkarian says.

This and other work suggests that there is an emotional component to chronic pain that is not necessarily involved in acute pain. Chronic pain and depression often coexist and reinforce one another. And some chronic pain can be eased with antidepressant drugs. But Wager cautions

that focusing on these links can be treacherous. Suggesting that pain is all in the head — even if that is technically the case — does not mean that it is imagined or faked. "People will always go to that black and white line," he says.

That line is a particular challenge in legal settings. "A person cannot be found disabled based on pain unless they can point to a specific cause," says Amanda Pustilnik, a legal expert at Harvard Law School in Cambridge, Massachusetts.

## ISOLATED INSTANCES

The United States sees tens of thousands of injury lawsuits every year, most of which involve claims of unresolved pain.

But that might be unusually high — countries with national health systems, such as Canada, see fewer lawsuits, says Davis. So far, the only pain case involving brain-imaging techniques known to have progressed to trial involved a truck driver named Carl Koch, whose wrist was burned by a glob of molten asphalt in 2005. A year later, he said he was still in pain and sued his former employer, Western Emulsions in Tucson, Arizona, for damages.

Koch had had his brain scanned by Joy Hirsch, a neuroscientist who was running the fMRI Research Center at Columbia University in New York City. Hirsch had developed a method that she says can "tap into" chronic pain. Lightly touching the affected wrist provoked a signal in sensory regions and other brain areas associated with pain; touching the other wrist did not. The test, she says, is a well-characterized way to distinguish allodynia — a pain response to a stimulus that does not normally cause pain — from imagined pain.

At the trial, Western Emulsions called Sean Mackey, a neurologist at Stanford University in Redwood City, California, as an expert witness. Mackey maintained that pain is too subjective to measure in this way and that the signature Hirsch was detecting could have been produced if Koch had expected to feel pain in the affected wrist or was unduly concentrating on it — deliberately or not. Hirsch argued that there are known signals for imagined pain that were not apparent in the scans.

Ultimately, the judge admitted the scan, and the case settled for \$800,000 — more than ten times the company's initial offering, according to Koch's lawyer, Roger Strassburg.

Another issue, Mackey says, is that it might be possible for people to cheat the test. In a 2005 study, he instructed volunteers to lie in an fMRI scanner and touch a hot plate while he showed them a video of flames that became more or less intense on the basis of their brain activity. Given this visual feedback, volunteers were able to control the intensity of the flames by imagining the pain as being more or less severe than it actually was<sup>3</sup>. Mackey is looking into the technique as a way to control chronic pain, but he is also studying whether people can trick the scanner.

After the Koch case, the use of such techniques began to pick up. Hirsch, who is now at Yale University in New Haven, Connecticut, says that while she was at Columbia, she had been doing two to three pain-related scans per month, many of which were to support lawsuits. She is hoping to offer the service at Yale.

A main criticism of the various techniques being used in civil suits is

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the paucity of publications to validate them. Hirsch has not published anything on her method, but says that she does not think it is necessary. The way in which different body parts are represented in the brain has been well mapped, she says, and the scans she has done provide no further insight than answering whether or not the person was in pain.

MMT takes a somewhat different approach: it compares scans before and after an individual engages in a painful activity. For example, Annie was scanned before and after walking around, and the company claimed that it could detect a clear pain signal in the second scan. But the company's only publication, led by co-founder and chief science officer Donald Marks, has been a single case study. After the person did something painful, a brain scan revealed particularly strong activity in the insula, which is involved in consciousness and self-regulation, and the somatosensory cortex, which processes sensations from the various parts of the body<sup>4</sup>.

These regions are involved in pain, but they are also involved in many other things. "If you went to a Society for Neuroscience meeting and walked into any non-pain-related slide session, you'd see the same regions being talked about," Davis says. Getting a patient such as Annie to walk around between scans would not only cause her pain, but also increase her awareness of her back, which would activate the insula. Davis, who does not think that pain imaging should be used in court for this purpose, says that she finds it disturbing that Marks's study cites her work, which measured a different kind of brain activity. "It's quite shocking for them to be quoting studies that don't back up their technology at all," she says.

Moreover, the test cannot be validated in a single person, Wager says. Any number of confounding factors — emotion, expectation, or head movement in the scanner, for instance — could account for the signals the company sees. To prove that the method is valid, the researchers would have to show that the signals differ between people in pain and controls, he says, and that there is a biological mechanism that accounts for the signal. Without that, "it's like reading tea leaves".

Marks disputes this, saying that numerous studies, including Wager's, have shown that fMRI can reliably distinguish between pain states. "My work is an application on an individual basis of all the data to date which validates this approach," Marks says. He also argues that the approach is not meant to determine whether or not someone who says they are in pain actually is, "I'm taking individuals that everyone agrees have pain and providing a visual graphic representation of that pain."

#### CLOSE TO MARKET

Using different techniques, Chronic Pain Diagnostics (CPD) of Roseville, California, is planning to offer commercial scans for litigants. CPD compares scans taken of a person's brain after they received an electric shock to a database of images from 30 individuals with and without chronic pain. People with chronic pain respond to a stimulus differently from healthy controls, and the company has developed an algorithm that allows it to distinguish between the two with 92% accuracy<sup>5</sup>. CPD president and co-founder Shaun England says that he expects a scan to cost between \$5,000 and \$6,000.

Mackey says that the application is interesting and potentially useful if the technique is replicated in larger groups. But Apkarian says the sample size is too small to determine meaningful differences at this point. Just as in MMT's technique, background signals such as head movement could confound the interpretation. "If you simply blindly use it, there is a very good chance you will always find a difference" between groups, he says.

CPD's executive research director, Daniel Callan, says that the company

has ways to control for outside factors that could affect its database, such as randomizing the order in which the patients are scanned and using people of different ages and genders. But he agrees that further experiments are needed to determine how well the algorithm works for individual patients. England says that the company hopes to start another study soon.

Scientists' concerns about the validity of pain scans might not matter much to legal professionals and the courts, says Michael Flomenhaft, an attorney in New York City who specializes in chronic pain and neuroimaging. "There's a lot of scientific information that can't be stated with the level of certainty you'd need to present it at a scientific conference, but is confident and valuable in a legal setting."

There is, however, evidence that brain scans could be overly persuasive to jurors. Research has suggested that the general public is more likely to

accept poor arguments if they are accompanied by neuroscientific evidence<sup>6</sup>. In the Koch case, Mackey says, "pretty brain pictures ended up being very compelling".

The efforts to introduce pain imaging are similar in some ways to attempts over the past decade to use fMRI as a lie detector. Most researchers question the reliability of this technique. It is difficult to validate because study volunteers tend not to have the same motivations to lie as criminal defendants. But that has not stopped several companies from trying — thus far unsuccessfully — to have the evidence introduced in US courts. Pain imaging has been more successful owing to richer research on the topic. And the stakes are much lower for a civil case than in a criminal trial, so the bar for what constitutes evidence is lower, according to an analysis in the *Journal of Law and the Biosciences*<sup>7</sup>.

But some scientists and ethicists are concerned about where the increasing acceptance of pain imaging might lead. Pustilnik worries that it could become a sort of pass-fail test, not just forcing litigants to provide proof of their pain, but potentially making it a requirement to get prescription medications or insurance coverage. She is heading a working group at Harvard that is developing a list of ethical and scientific standards for the technologies before they become widespread.

Levy and Marks insist that their technology is not capable of that. "Fundamentally, we can't prove that a patient does not have pain," Levy says, because an individual might still be experiencing pain even if the scanner does not show it.

But that situation may be inevitable, says Stuart Derbyshire, a neuroscientist at the National University of Singapore. "If we accept the logic that the brain imager knows, then we have to accept that it's going to win even in cases when we don't want it to."

Even so, many say that the research should continue to strive for application, including inside the courtroom. "We already make many wrong treatment and legal decisions about who is and is not in pain and who shouldn't be believed," Wager says. "If we had new information, that could help us do a better job." ■ SEE EDITORIAL P.456

Sara Reardon writes for Nature from Washington DC.

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