

Quartz

We're terrible at measuring other people's pain—but researchers think there is a better way to treat it

By John Walsh
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How much does it hurt? *AP Photo/Rajesh Kumar Singh*

One night in May, my wife sat up in bed and said, “I’ve got this awful pain just here.” She prodded her abdomen and made a face. “It feels like something’s really wrong.” Woozily noting that it was 2am, I asked what kind of pain it was. “Like something’s biting into me and won’t stop,” she said.

“Hold on,” I said blearily, “help is at hand.” I brought her a couple of ibuprofen with some water, which she downed, clutching my hand and waiting for the ache to subside.

An hour later, she was sitting up in bed again, in real distress. “It’s worse now,” she said, “really nasty. Can you phone the doctor?” Miraculously, the family doctor answered the phone at 3am, listened to her recital of symptoms and concluded, “It might be your appendix. Have you had yours taken out?” No, she hadn’t. “It could be appendicitis,” he surmised, “but if it was dangerous you’d be in much worse pain than you’re in. Go to the hospital in the morning, but for now, take some paracetamol and try to sleep.”

Barely half an hour later, the balloon went up. She was awakened for the third time, but now with a pain so savage and uncontrollable it made her howl like a tortured witch face down on a bonfire. The time for murmured assurances and spousal procrastination was over. I rang a local minicab, struggled into my clothes, bundled her into a dressing gown, and we sped to St Mary’s Paddington at just before 4am.

The flurry of action made the pain subside, if only through distraction, and we sat for hours while doctors brought forms to be filled, took her blood pressure and ran tests. A registrar poked a needle into my wife’s wrist and said, “Does that hurt? Does that? How about *that*?” before concluding: “Impressive. You have a very high pain threshold.”

The pain was from pancreatitis, brought on by rogue gallstones that had escaped from her gall bladder and made their way, like fleeing convicts, to a refuge in her pancreas, causing agony. She was given a course of antibiotics and, a month later, had an operation to remove her gall bladder.

“It’s keyhole surgery,” said the surgeon breezily, “so you’ll be back to normal very soon. Some people feel well enough to take the bus home after the operation.” His optimism was misplaced. My lovely wife, she of the admirably high pain threshold, had to stay overnight, and came home the following day filled with painkillers; when they wore off, she writhed with suffering. After three days she rang the specialist, only to be told: “It’s not the operation that’s causing discomfort—it’s the air that was pumped inside you to separate the organs before surgery.” Like all too many surgeons, they had lost interest in the fallout once the operation had proved a success.

During that period of convalescence, as I watched her grimace and clench her teeth and let slip little cries of anguish until a long regimen of combined ibuprofen and codeine finally conquered the pain, several questions came into my head. Chief among them was: Can anyone in the medical profession talk about pain with any authority? From the family doctor to the surgeon, their remarks and suggestions seemed tentative, generalized, unknowing—and potentially dangerous: Was it right for the doctor to tell my wife that her level of pain didn’t sound like appendicitis when the doctor didn’t know whether she had a high or low pain threshold? Should he have advised her to stay in bed and risk her appendix exploding into peritonitis? How could surgeons predict that patients would feel only “discomfort” after such an operation when she felt agony—an agony that was aggravated by fear that the operation had been a failure?

I also wondered if there were any agreed words that would help a doctor understand the pain felt by a patient. I thought of my father, a GP in the 1960s with an NHS practice in south London, who used to marvel at the colourful pain symptoms he heard: “It’s like I’ve been attacked with a stapler”; “like having rabbits running up and down my spine”; “it’s like someone’s opened a cocktail umbrella in my penis...” Few of them, he told me, corresponded to the symptoms listed in a medical textbook. So how should he proceed? By guesswork and aspirin?

There seemed to be a chasm of understanding in human discussions of pain. I wanted to find out how the medical profession apprehends pain—the language it uses for something that’s invisible to the naked eye, that can’t be measured except by asking for the sufferer’s subjective description, and that can be treated only by the use of opium derivatives that go back to the Middle Ages.

When investigating pain, the basic procedure for clinics everywhere is to give a patient the McGill Pain Questionnaire. This was developed in the 1970s by two scientists, Dr. Ronald Melzack and Dr. Warren Torgerson, both of McGill University in Montreal, and is still the main tool for measuring pain in clinics worldwide.

Melzack and his colleague Dr. Patrick Wall of St Thomas' Hospital in London had already galvanized the field of pain research in 1965 with their seminal 'gate control theory', a ground-breaking explanation of how psychology can affect the body's perception of pain. In 1984 the pair went on to write *Wall and Melzack's Textbook of Pain*, the most comprehensive reference work in pain medicine. It's gone through five editions and is currently over 1,000 pages long.

In the early 1970s, Melzack began to list the words patients used to describe their pain and classified them into three categories: sensory (which included heat, pressure, "throbbing" or "pounding" sensations), affective (which related to emotional effects, such as "tiring," "sickening," "grueling" or "frightful") and lastly evaluative (evocative of an experience – from "annoying" and "troublesome" to "horrible," "unbearable" and "excruciating").

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You don't have to be a linguistic genius to see there are shortcomings in this lexical smorgasbord. For one thing, some words in the affective and evaluative categories seem interchangeable—there's no difference between "frightful" in the former and "horrible" in the latter, or between "tiring" and "annoying"—and all the words share an unfortunate quality of sounding like a duchess complaining about a ball that didn't meet her standards.

But Melzack's grid of suffering formed the basis of what became the McGill Pain Questionnaire. The patient listens as a list of "pain descriptors" is read out and has to say whether each word describes their pain—and, if so, to rate the intensity of the feeling. The clinicians then look at the questionnaire and put check marks in the appropriate places. This gives them a number, or a percentage figure, to work with in assessing, later, whether a treatment has brought the patient's pain down (or up).

A more recent variant is the National Initiative on Pain Control's Pain Quality Assessment Scale (PQAS), in which patients are asked to indicate, on a scale of 1 to 10, how "intense"—or "sharp," "hot," "dull," "cold," "sensitive," "tender," "itchy," etc.—their pain has been over the past week.

The trouble with this approach is the imprecision of that scale of 1 to 10, where a 10 would be "the most intense pain sensation imaginable." How does a patient "imagine" the worst pain ever and give their own pain a number? Middle-class British men who have never been in a war zone may find it hard to imagine anything more agonizing than toothache or a tennis injury. Women who have experienced childbirth may, after that experience, rate everything else as a mild 3 or 4.

I asked some friends what they thought the worst physical pain might be. Inevitably, they just described nasty things that had happened to them. One man nominated gout. He recalled lying on a sofa, with his gouty foot resting on a pillow, when a visiting aunt

passed by; the chiffon scarf she was wearing slipped from her neck and lightly touched his foot. It was “unbearable agony.” A brother-in-law nominated post-root canal toothache—unlike muscular or back pain, he said, it couldn’t be alleviated by shifting your posture. It was “relentless.” A male friend confided that a haemorrhoidectomy had left him with irritable bowel syndrome, in which a daily spasm made him feel “as if somebody had shoved a stirrup pump up my arse and was pumping furiously.” The pain was, he said, “boundless, as if it wouldn’t stop until I exploded.” A woman friend recalled the moment the hem of her husband’s trouser leg snagged on her big toe, ripping the nail clean off. She used a musical analogy to explain the effect: “I’d been through childbirth, I’d broken my leg—and I recalled them both as low moaning noises, like cellos; the ripped-off nail was excruciating, a great, high, deafening shriek of psychopathic violins, like nothing I’d heard—or felt—before.”

A novelist friend who specializes in World War I drew my attention to Stuart Cloete’s memoir *A Victorian Son* (1972), in which the author records his time in a field hospital. He marvels at the stoicism of the wounded soldiers: “I have heard boys on their stretchers crying with weakness, but all they ever asked for was water or a cigarette. The exception was a man hit through the palm of the hand. This I believe to be the most painful wound there is, as the sinews of the arm contract, tearing as if on a rack.”

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Is it true? Looking at the Crucifixion scene in Matthias Grünewald’s *Isenheim Altarpiece* (1512–16), you take in the horribly straining fingers of Christ, twisted around the fat nailheads that skewer his hands to the wood—and oh, God yes, you believe it *must* be true.

It seems a shame that these eloquent descriptions are reduced by the McGill Questionnaire to words like “throbbing” or “sharp,” but its function is simply to give pain a number—a number that will, with luck, be decreased after treatment, when the patient is reassessed.

This procedure doesn’t impress professor Stephen McMahon of the London Pain Consortium, an organization formed in 2002 to promote internationally competitive research into pain. “There are lots of problems that come with trying to measure pain,” he says. “I think the obsession with numbers is an oversimplification. Pain is not unidimensional. It doesn’t just come with scale—a lot or a little—it comes with other baggage: how threatening it is, how emotionally disturbing, how it affects your ability to concentrate. The measuring obsession probably comes from the regulators who think that, to understand drugs, you have to show efficacy. And the American Food and Drug Administration don’t like quality-of-life assessments; they like hard numbers. So we’re thrown back on giving it a number and scoring it. It’s a bit of a wasted exercise because it’s only one dimension of pain that we’re capturing.”

Pain can be either acute or chronic, and the words do not (as some people think) mean “bad” and “very bad.” Acute pain means a temporary or one-off feeling of discomfort, which is usually treated with drugs; chronic pain persists over time and has to be lived with as a malevolent everyday companion. But because patients build up a resistance to drugs, other forms of treatment must be found for it.

The Pain Management and Neuromodulation Centre at Guy’s and St Thomas’ Hospital in central London is the biggest pain center in Europe. Heading the team there is Dr. Adnan Al-Kaisy, who studied medicine at the University of Basrah, Iraq, and later worked in anaesthetics at specialist centers in England, the USA and Canada.

Who are his patients and what kind of pain are they generally suffering from? “I’d say that 55% to 60% of our patients suffer from lower back pain,” he says. “The reason is, simply, that we don’t pay attention to the demands life makes on us, the way we sit, stand, walk and so on. We sit for hours in front of a computer, with the body putting heavy pressure on small joints in the back.” Al-Kaisy reckons that in the UK, the incidence of chronic lower back pain has increased substantially in the last 15–20 years, and that “the cost in lost working days is about £6–7 billion”.

Elsewhere, the clinic treats those suffering from severe chronic headaches and injuries from accidents that affect the nervous system.

Do they still use the McGill Questionnaire? “Unfortunately yes,” says Al-Kaisy. “It’s a subjective measurement. But pain can be magnified by a domestic argument or trouble at work, so we try to find out about the patient’s life—their sleeping patterns, their ability to walk and stand, their appetite. It’s not just the patient’s condition, it’s also their environment.”

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The challenge is to transform this information into scientific data. “We’re working with professor Raymond Lee, chair of biomechanics at the South Bank University, to see if there can be objective measurement of a patient’s disability due to pain,” he says. “They’re trying to develop a tool, rather like an accelerometer, which will give an accurate impression of how active or disabled they are, and tell us the cause of their pain from the way they sit or stand. We’re really keen to get away from just asking the patient how bad their pain is.”

Some patients arrive with pains that are far worse than backache and require special treatment. Al-Kaisy describes one patient—let us call him Carter—who suffered from a terrible condition called ilioinguinal neuralgia, a disorder that produces a severe burning and stabbing pain in the groin. “He’d had an operation in the testicular area, and the inguinal nerve had been cut. The pain was excruciating: when he came to us, he was on four or five different medications, opiates with very high dosages, anticonvulsive medication, opioid patches, paracetamol and ibuprofen on top of that. His life was turned

upside down, his job was on the line.” The utterly stricken Carter was to become one of Al-Kaisy’s big successes.

Since 2010, Guy’s and St Thomas’ has offered a residential program for adults whose chronic pain hasn’t responded to treatment at other clinics. The patients come in for four weeks, away from their normal environment, and are seen by a motley crew of psychologists, physiotherapists, occupational health specialists and nursing physicians who between them devise a program to teach them strategies for managing their pain.

Many of these strategies come under the heading of “neuromodulation,” a term you hear everywhere in pain management circles. In simple terms, it means distracting the brain from constantly brooding on the pain signals it’s getting from the body’s “periphery.” Sometimes the distraction is a cunningly deployed electric shock.

“We were the first center in the world to pioneer spinal cord stimulation,” says Al-Kaisy proudly. “In pain occasions, overactive nerves send impulses from the periphery to the spinal cord and from there to the brain, which starts to register pain. We try to send small bolts of electricity to the spinal cord by inserting a wire in the epidural area. It’s only one or two volts, so the patient feels just a tingling sensation over where the pain is, instead of feeling the actual pain. After two weeks, we give the patient an internal power battery with a remote control, so he can switch it on whenever he feels pain and carry on with his life. It’s essentially a pacemaker that suppresses the hyperexcitability of nerves by delivering subthreshold stimulation. The patient feels nothing except his pain going down. It’s not invasive—we usually send patients home the same day.”

When Carter, the chap with the agonized groin, had failed to respond to any other treatments, Al-Kaisy tried his box of tricks. “We gave him something called a dorsal root ganglion stimulation. It’s like a small junction-box, placed just underneath one of the bones of the spine. It makes the spine hyperexcited, and sends impulses to the spinal cord and the brain. I pioneered a new technique to put a small wire into the ganglion, connected to an external power battery. Over ten days the intensity of pain went down by 70%—by the patient’s own assessment. He wrote me a very nice email saying I had changed his life, that the pain had just stopped completely, and that he was coming back to normality. He said his job was saved, as was his marriage, and he wanted to go back to playing sport. I told him, ‘Take it easy. You mustn’t start climbing the Himalayas just yet.’” Al-Kaisy beams. “This is a remarkable outcome. You cannot get it from any other therapies.”

The greatest recent breakthrough in assessing pain, according to professor Irene Tracey, head of the University of Oxford’s Nuffield Department of Clinical Neurosciences, has been the understanding that chronic pain is a thing in its own right. She explains: “We always thought of it as acute pain that just goes on and on—and if chronic pain is just a continuation of acute pain, let’s fix the thing that caused the acute and the chronic should go away. That has spectacularly failed. Now we think of chronic pain as a shift to another

place, with different mechanisms, such as changes in genetic expression, chemical release, neurophysiology and wiring. We've got all these completely new ways of thinking about chronic pain. That's the paradigm shift in the pain field."

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Tracey has been called the "Queen of Pain" by some media commentators. She was, until recently, the Nuffield Professor of Anaesthetic Science and is an expert in neuroimaging techniques that explore the brain's responses to pain. Despite her nickname, in person she is far from alarming: a bright-eyed, enthusiastic, welcoming and hectically fluent woman of 50, she talks about pain at a personal level. She has no problem defining the "ultimate pain" that scores 10 on the McGill Questionnaire: "I've been through childbirth three times, and my 10 is a very different 10 from before I had kids. I've got a whole new calibration on that scale." But how does she explain the ultimate pain to people who haven't experienced childbirth? "I say, 'Imagine you've slammed your hand in a car door – that's 10.'"

She uses a personal example to explain the way perception and circumstance can alter the way we experience pain, as well as the phenomenon of "hedonic flipping," which can convert pain from an unpleasant sensation into something you don't mind. "I did the London Marathon this year. It needs a lot of training and running and your muscles ache, and next day you're really in pain, but it's a nice pain. I'm no masochist, but I associate the muscle pain with thoughts like, 'I did something healthy with my body,' 'I'm training,' and 'It's all going well.'"

I ask her why there seems to be a gap between doctors' and patients' apprehension of pain. "It's very hard to understand, because the system goes wrong from the point of injury, along the nerve that's taken the signal into the spinal cord, which sends signals to the brain, which sends signals back, and it all unravels with terrible consequential changes. So my patient may be saying, 'I've got this excruciating pain here,' and I'm trying to see where it's coming from, and there's a mismatch here because you can't see any damage or any oozing blood. So we say, 'Oh come now, you're obviously exaggerating, it can't be as bad as that.' That's wrong—it's a cultural bias we grew up with, without realizing."

Recently, she says, there has been an explosion of understanding about how the brain is involved in pain. Neuroimaging, she explains, helps to connect the subjective pain with the objective perception of it. "It fills that space between what you can see and what's being reported. We can plug that gap and explain why the patient is in pain even though you can't see it on your X-ray or whatever. You're helping to bring truth and validity to these poor people who are in pain but not believed."

But you can't simply "see" pain glowing and throbbing on the screen in front of you. "Brain imaging has taught us about the networks of the brain and how they work," she says. "It's not a pain-measuring device. It's a tool that gives you fantastic insight into the

anatomy, the physiology and the neurochemistry of your body and can tell us why you have pain, and where we should go in and try to fix it.”

Some of the ways in, she says, are remarkably direct and mechanical—like Al-Kaisy’s spinal cord stimulation wire. “There are now devices you can attach to your head and allow you to manipulate bits of the brain. You can wear them like bathing caps. They’re portable, ethically allowed brain-simulation devices. They’re easy for patients to use and evidence is coming, in clinical trials, that they are good for strokes and rehabilitation. There’s a parallel with the games industry, where they’re making devices you can put on your head so kids can use thought to move balls around. The games industry is, for fun, driving this idea that when you use your brain, you generate electrical activities. They’re developing the technology really fast, and we can use it in medical applications.”

According to the International Association for the Study of Pain, pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” It’s a broad-brush definition that hints at the holistic nature of pain and the range of factors that might influence our perception of it. If not all of its causes are directly physical, standardized drug treatments will always be something of a blunt instrument.

Researchers at the Human Pain Research Laboratory at Stanford University, California, are working to gain a better understanding of individual responses to pain so that treatments can be more targeted. The center was created in 1995 by the pleasingly named Dr Martin Angst of the Department of Anesthesiology. Its first investigations were into finding reliable methods of quantifying pain. Then Angst (assisted by the equally pleasingly named Dr Martha Tingle) looked into questions of opiate pharmacology, such as how easily the body builds up toleration to drugs.

Pain has become a huge area of medical research in the USA, for a simple reason. Chronic pain affects over 100 million Americans and costs the country over half a trillion dollars a year in lost working hours, which is why it’s become a magnet for funding by big business and government.

The laboratory has several study initiatives on the go—into migraine, fibromyalgia, facial pain and other conditions – but its largest is into back pain. It has been endowed with a \$10m grant from the National Institutes of Health to study non-drug alternative treatments for lower back pain. The specific treatments are mindfulness, acupuncture, cognitive behavioural therapy and real-time neural feedback. This may seem a very Californian range of pursuits, but the lab takes them very seriously and is enlisting an army of patients to build up a massive database.

They plan to inspect the pain tolerance of 400 people over five years of study, ranging from pain-free volunteers to the most wretched chronic sufferers who have been to other specialists but found no relief. Subjects are all called in, given screening tests (to exclude

those with abnormal drug regimens or excessive “suicidality”) then subjected to several quantitative sensory tests: participants are asked to immerse one naked foot in a bucket of iced water until they feel pain; then one arm is subjected to a ‘contact heat evoked potential simulator,’ which gradually heats up small-diameter nerve fibers until the patient feels pain; then they have pressure needles poked onto their skin without breaking it until they report discomfort.

In all three cases, the idea is to find people’s mid-range tolerance (they’re asked to rate their pain while they’re experiencing it), to establish a usable baseline. They then are given the non-invasive treatments—mindfulness, acupuncture, etc—and are subjected afterwards to the same pain stimuli, to see how their pain tolerance has changed from their baseline reading. MRI scanning is used on the patients in both laboratory sessions, so that clinicians can see and draw inferences from the visible differences in blood flow to different parts of the brain.

A remarkable feature of the assessment process is that patients are also given scores for psychological states: a scale measures their level of depression, anxiety, anger, physical functioning, pain behaviour and how much pain interferes with their lives. This should allow physicians to use the information to target specific treatments. All these findings are stored in an ‘informatics platform’ called CHOIR, which stands for the Collaborative Health Outcomes Information Registry. It has files on 15,000 patients, 54,000 unique clinic visits and 40,000 follow-up meetings.

The big chief at the Human Pain Research Laboratory is Dr. Sean Mackey, Redlich Professor of Anesthesiology, Perioperative and Pain Medicine, Neurosciences and Neurology at Stanford. His background is in bioengineering, and under his governance the Stanford Pain Management Center has twice been designated a centre of excellence by the American Pain Society. A tall, genial, easy-going man, he is sometimes approached by legal firms who want him to appear in court to state definitively whether their client is or isn’t in chronic pain (and therefore justified in claiming absentee benefit). His response is surprising.

“In 2008, I was asked by a law firm to speak in an industrial injury case in Arizona. This poor guy got hot burning asphalt sprayed on his arm at work; he had a claim of burning neuropathic pain. The plaintiff’s side brought in a cognitive scientist, who scanned his brain and said there was conclusive evidence that he had chronic pain. The defence asked me to comment, and I said, ‘That’s hogwash, we cannot use this technology for that purpose.’

“Shortly afterwards, I gave a talk on pain, neuroimaging and the law, explaining why you can’t do this—because there’s too much individual variability in pain, and the technology isn’t sensor-specific enough. But I concluded by saying, ‘If you *were* to do this, you’d use modern machine-learning approaches, like those used for satellite reconnaissance to determine whether a satellite is seeing a tank or a civilian truck.’ Some of my students said, ‘Can you give us some money to try this?’ I said, ‘Yes, but it can’t be done.’ But

they designed the experiment—and discovered that, using brain imagery, they could predict with 80% accuracy whether someone was feeling heat pain or not.”

Mackey finally published a paper about the experiment. So did his findings influence any court decisions? “No. I get asked by attorneys, and I always say, ‘There is no place for this in the courtroom in 2016 and there won’t be in 2020. People want to push us into saying this is an objective biomarker for detecting that someone’s in pain. But the research is in carefully controlled laboratory conditions. You cannot generalize about the population as a whole. I told the attorneys, ‘This is too much of a leap.’ I don’t think there’s a lot of clinical utility in having a pain-o-meter in a court or in most clinical situations.”

Mackey explains the latest thinking about what pain actually is. “Now we understand that pain is a balance between ascending information coming from our bodies and descending inhibitory systems from our brains. We call the ascending information ‘nociception’—from the Latin *nocere*, to harm or hurt—meaning the response of the sensory nervous system to potentially harmful stimuli coming from our periphery, sending signals to the spinal cord and hitting the brain with the perception of pain. The descending systems are inhibitory, or filtering, neurons, which exist to filter out information that’s not important, to ‘turn down’ the ascending signals of hurt. The main purpose of pain is to be the great motivator, to tell you to pay attention, to focus. When Martin was doing the pain lab, we had no way of addressing these two dynamic systems, and now we can.”

Mackey is immensely proud of his massive CHOIR database—which records people’s pain tolerance levels and how they are affected by treatment—and has made it freely available to other pain clinics as a ‘community source platform’, collaborating with academic medical centers nationwide “so that a rising tide elevates all boats.” But he’s also humble enough to admit that science can’t tell us which are the sites of the body’s worst pains.

“Back pain is the most reported pain at 28%, but I know there’s a higher density of nerve fibers in the hands, face, genitals and feet than in other areas. And there are conditions where the sufferer has committed suicide to get away from the pain: things like post-herpetic neuralgia, that burning nerve pain that occurs after an outbreak of shingles and is horrific; another is cluster headaches—some patients have thought about taking a drill to their heads to make it stop.”

Like Irene Tracey, he’s enthusiastic about the rise of transcranial magnetic stimulation (“Imagine hooking a nine-volt battery across your scalp”) but, when asked about his particular successes, he talks about simple solutions. “Early on in my career, I used to be very focused on the peripheral, the apparent site of the pain. I was doing interventions, and some people would get better but a lot wouldn’t. So I started listening to their fears and anxieties and working on those, and became very brain-focused. I noticed that if you have a nerve trapped in your knee, your whole leg could be on fire, but if you apply a local anaesthetic there, it could abolish it.

“This young woman came to me with a terrible burning sensation in her hand. It was always swollen; she couldn’t stand anyone touching it because it felt like a blowtorch.” Mackey noticed that she had a post-operative scar from prior surgery for carpal tunnel syndrome. Speculating that this was at the root of her problem, he injected Botox, a muscle relaxant, at the site of the scar. “A week later, she came up and gave me this huge hug and said, ‘I was able to pick up my child for the first time in two years. I haven’t been able to since she was born.’ All the swelling was gone. It taught me that it’s not all about the body part, and not all about the brain. It’s about both.” How counterintuitive to discover that, after centuries of curing pain with opiates, the mind can give the morphine a run for its money.