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THE AUTHOR OPENS
HER MIND
AND TAKES A LOOK.

MY PAIN, MY BRAIN

BY MELANIE THERNSTROM

WHO HASN'T WISHED she could watch her brain at work and make changes to it, the way a painter steps back from a painting, studies it and decides to make the sky a different hue? If only we could spell-check our brain like a text, or reprogram it like a computer to eliminate glitches like pain, depression and learning disabilities. Would we one day become completely transparent to ourselves, and — fully conscious of consciousness — consciously create ourselves as we like?

The glitch I'd like to program out of my brain is chronic pain. For the past 10 years, I have been suffering from an arthritic condition that causes chronic pain in my neck that radiates into the right side of my face and right shoulder and arm. Sometimes I picture the pain — soggy, moldy, dark or perhaps ashy, like those alarming pictures of smokers' lungs. Wherever the pain is located, it must look awful by now, after a decade of dominating my brain. I'd like to replace my forehead with a Plexiglas window, set up a camera and film my brain and (since this is my brain, I'm the director) redirect it. Cut. Those areas that

Illustrations by Marcos Chin
are generating pain — cool it. Those areas that are supposed to be alleviating pain — hello? I need you! Down-regulate pain-perception circuitry, as scientists say. Up-regulate pain-modulation circuity. Now.

RECENTLY, I HAD a glimpse of what that reprogramming would look like. I was lying on my back in a large white plastic F.M.R.I. machine that uses ingenious new software, peering up through 3-D goggles at a small screen. I was experiencing a clinical demonstration of a new technology — real-time functional neuroimaging — used in a Stanford University study, now in its second phase, that allows subjects to see their own brain activity while feeling pain and to try to change that brain activity to control their pain.

Over six sessions, volunteers are being asked to try to increase and decrease their pain while watching the activation of a part of their brain involved in pain perception and modulation. This real-time imaging lets them assess how well they are succeeding. Dr. Sean Mackey, the study’s senior investigator and the director of the Neuroimaging and Pain Lab at Stanford, explained that the results of the study’s first phase, which were recently published in the prestigious Proceedings of the National Academy of Sciences, showed that while looking at the brain, subjects can learn to control its activation in a way that regulates their pain. While this may be likened to biofeedback, traditional biofeedback provides indirect measures of brain activity through information about heart rate, skin temperature and other autonomic functions, or even EEG waves. Mackey’s approach allows subjects to interact with the brain itself.

“It is the mind-body problem — right there on the screen,” one of Mackey’s collaborators, Christopher deCharms, a neurophysiologist and a principal investigator of the study, told me later. “We are doing something that people have wanted to do for thousands of years. Descartes said, ‘I think, therefore I am.’ Now we’re watching that process as it unfolds.”

Suddenly, the machine made a deep rattling sound, and an image flickered before me: my brain. I am looking at my own brain, as it thinks my own thoughts, including these thoughts.

How does it work? I want to ask. Just as people were once puzzled by Freud’s talking cure (how does describing problems solve them?), the Stanford study makes us wonder: How can one part of our brain control another by looking at it? Who is the “me” controlling my brain, then? It seems to deepen the mind-body problem, widening the old Cartesian divide by splitting the self into subject and agent.

But most of all I want to know: Will I be able to learn it?

Perhaps more than any other aspect of human existence, persistent pain is experienced as something we cannot control but desperately wish we could. Acute pain serves the evolutionary function of warning us of tissue damage, but chronic pain does nothing except undo us. Pain is the primary complaint that sends people to the doctor. Of the 50-odd million sufferers in the United States, half cannot get adequate relief from their chronic pain. Many do not even have a diagnosis.

Unlike acute pain, chronic pain is now thought to be a disease of the central nervous system that may or may not correlate with any tissue damage but involves an errant reprogramming in the brain and spinal cord. The brain can generate terrible pain in a wound that is long healed, in a body that is numb and paralyzed or — in the case of phantom-limb pain — in a limb that no longer even exists.

Although there have been many theories about how pain works in the brain, it is only through neuroimaging that the process has actually been observed. It is now clear that there is no single pain center in the brain. Rather, pain is a complex, adaptive network involving 5 to 10 areas of the brain transmitting information back and forth.

This network has two pain systems: pain perception and pain modulation, which involve both overlapping and distinct brain structures. The pain-modulatory system constantly interacts with the pain-perception system, inhibiting its activity. Much chronic pain is thought to involve either an overactive pain-perception circuit or an underactive pain-modulation circuit.

LIKE EVERYONE who suffers from chronic pain, I find it hard to believe that I have a pain-modulation circuit. The aspect of my pain I feel most certain about is that it is not voluntary: I cannot modulate it. And this belief is reinforced every single day that I suffer from pain, which is every day. Yet I know that pain is not a fact, like a broken bone; it’s a perception, like hunger, about a physical state (“an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage,” as the International Association for the Study of Pain defines it). And it’s a mercurial perception; under certain circumstances the pain-modulatory system works like a spell and the brain completely blocks out pain.

Soldiers, athletes, martyrs and pilgrims engage in battles, athletic feats or acts of devotion without being distracted by the pain of injuries. When the teenage surfer Bethany Hamilton’s arm was bitten off by a shark, she felt pressure, but “I didn’t feel any pain — I’m really lucky, because if I felt pain, things might not have gone as well,” she said (articulating one reason the modulatory system evolved: if she had thrashed about in pain, she would have bled until she drowned).

In addition to being activated by stress, the pain-modulatory system is triggered by belief. The brain will shut down pain if it believes it has been given pain relief, even when it hasn’t (the placebo effect), and it will augment pain if it believes you are being hurt, even if you aren’t (the nocebo effect).

The brain’s modulatory system relies on endogenous endorphins, its own opiatelike substances. The nature of a placebo has long been a source of speculation and debate, but neuroimaging studies have shown the way a placebo actually helps to activate the pain-modulatory system.

In a recently published study led by Dr. Jon-Kar Zubieta at the University of Michigan Medical School, the brains of 14 men were imaged after a stinging saltwater solution was injected into their jaws. They were then each given a placebo and told that it would positively relieve their pain. The men immediately felt better — and the screen showed how. Parts of the brain that release endogenous opiates lighted up. In other words, fake opiates caused the brain to dispense real ones. Like some New Age diagram, philosophy becomes chemistry; believing becomes reality; the mind unites with the body.

Other studies have shown that opiates and other medications rely on a placebo to achieve part of their effect. When subjects are covertly given strong opiates like morphine, they don’t work nearly as well as they do if the subjects are told they are being given a powerful pain reliever. Even

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real medications require some of the brain’s own bounty.

Conversely, thinking about pain creates pain. In studies at Oxford University, Irene Tracey has shown that asking subjects to think about their chronic pain, for example, increases activation in their pain-perception circuits. Distraction, on the other hand, is a great analgesic; when Tracey’s volunteers were asked to engage in a complicated counting task while being subjected to a painful heat stimulus, she could watch the pain-perception matrix decrease while cognitive parts of the brain involved in counting lighted up. At McGill University, Catherine Bushnell has shown that simply listening to tones while being subjected to a heat stimulus decreased activity in the pain-perception circuit.

“There is an interesting irony to pain,” comments Christopher deChams, who worked with Mackey designing and carrying out the Stanford study. We were talking in his office at Omneuron, a Menlo Park medical-technology company he founded three years ago to develop clinical applications of neuroimaging. “Everyone is born with a system designed to turn off pain. There isn’t an obvious mechanism to turn off other diseases like Parkinson’s. With pain, the system is there, but we don’t have control over the dial.”

The goal of the Stanford technique is to teach people to control their dials — to activate their modulatory systems without requiring the extreme stress of fleeing from a shark or the deception of a placebo. The hope of neuroimaging therapy (as deChams calls the Stanford technique) is that repeated practice will strengthen and eventually change the ineffective modulatory system to eliminate chronic pain, the way long-term physical therapy can change muscular weakness. The scan would thus be more than a research tool: the scan itself would be the treatment, and the subject his or her own researcher.

ONLY ONCE do I recall having a glimmer of my own pain-modulatory system at work: a hidden power that emerged, dispensed with pain and then returned to some forgotten fold in my brain, where I have never been able to locate it again. The event did not take place on a battlefield or a marathon course or in a temple; it was in a basement of the Stanford University medical center three years ago. At the time, Mackey had designed an earlier study that did not use imaging technology but focused on how suggestion alters pain perception. Although I was not formally enrolled in the study, I asked if I could undergo a clinical demonstration. My experience illustrated the power of suggestion in an unexpected fashion.

A metal probe attached to the underbelly of my arm heated up and cooled down at set intervals. I was told that although the heat probe would feel uncomfortable, my skin would not be burned. During one exposure, I was instructed to think of the pain as positively as possible, during another to think of it as negatively. After each sequence, I was asked to rate my pain on a 0-to-10 scale, with 10 being the worst pain I could imagine.

Although I discovered that I could make the pain fluctuate depending on whether I was imagining that I was sunbathing or was the victim of an inquisition, I still rated all the pain as low — ranging from 1 to 3. If 10 was being slowly burned alive, I felt I should at least be begging for mercy to justify a rating of 5. So I insisted that Mackey turn up the dial so I could get a real response. But even during the moments when I was actively trying to imagine the pain as negatively as possible, it remained in a mental box of “not even burned,” which kept it from really hurting; hurting, that is, the way a burn would.

As it turned out, I got a second-degree burn that later darkened into a square mark. Mackey was more than a little dismayed as we watched the reddening skin pucker, but I was thrilled. Naturally the protocol had been carefully designed not to injure anyone, yet in my case that protection had failed because of the very phenomenon it was designed to study: expectation — the effect of the mind on pain or placebo.

I had recently spent several weeks observing Mackey in the university’s pain clinic, where he is associate director. I was so convinced that Mackey — then a tall sandy-haired 39-year-old with a deep interest in technology (he got a Ph.D. in electrical engineering before he went to medical school) and an air of radiant integrity — would not burn me that my brain had not perceived the stimulus as a threat and generated pain. I admired him, I trusted him, I was positive that he wouldn’t hurt me. And, ipso facto, he hadn’t.

Mackey’s genius as a practitioner, I thought, lay partly in his ability to similarly inspire patients. “When I started working with pain patients, I realized how much of the treatment involved trying to reverse learned helplessness,” he said — to rally them out of the despair ingrained from years of unremitting pain and cajole their minds to chip in its own analgesic to their therapies. “The purpose of this study is to show patients their mind matters,” Mackey said.

The mark of the burn is barely visible now, but for a couple of years afterward, at times when my chronic pain was making me miserable, the sight of it would both encourage and reproach me. Here is the ultimate proof that my mind can control pain, I would think, yet I didn’t know how to make it wake up and do so. I could take the edge off the pain by conjuring positive images, but the effects didn’t last, and I never again had the remarkable placebo response that marked a second-degree burn. In fact, a mild burn from spilling tea on my hand one day brought tears to my eyes.

When the real-time neuroimaging study began, I couldn’t wait to try it.

THE AREA OF the brain that the scanner focuses on is the rostral anterior cingulate cortex (rACC). The rACC (a quarter-size patch in the middle-front of the brain, the cingulate cortex) plays a critical role in the awareness of the nastiness of pain: the feeling of dislike for it, a loathing so intense that you are immediately compelled to try to make it stop. Indeed, the pain of pain, you might say, its defining element, is the way in which the sensation is suffused with a particular unpleasantness researchers refer to as dysphoria. Since pain is a perception, it’s not pain if you don’t experience it as hurting. You can feel hot or cold or pressure, and note them simply as stimuli, but when they exceed a certain intensity, the rACC kicks in, and suddenly they become painful, riveting your attention and causing you to recoil.

Many pain-reducing techniques aim to manipulate the conscious awareness of pain. Distraction, placebo, meditation, imagining pleasant scenes and hypnosis all result in a reduction of rACC activation when they work. Patients who have undergone a radical surgical treatment occasionally used for pain (as well as for mental illness) called a cingulotomy, in which the rACC is partly destroyed, report that they are still aware of pain but that they don’t “mind” it anymore. Their emotional response has receded.

The image I saw while lying in the f.M.R.I. machine at the time of the recent Stanford study was not literally my rACC but a visual analogue of it that is easier to see: a 3-D image of a fire. The flames represent the degree of activation in your rACC: when it is low, the flames are low; when rACC activation is high, the flames flare. The study involves five 13-minute scanning runs, each consisting of five cycles of a 30-second rest.
followed by a 1-minute interval in which you try to increase rACC activation and then a 1-minute interval in which you try to decrease rACC activation.

Before my scan began, I was prepped in different mental strategies for increasing and modulating my pain. Everyone’s brain works a bit differently, though, so subjects have to experiment in the scanner to see what is most effective for them. For some, trying to distract themselves from their pain works best; for others, focusing on their pain — like embracing a Zen koan — seems to be what triggers their pain-modulatory system. When deCharms used neuroimaging therapy on himself to try to alleviate his chronic neck pain, he concentrated on the pain itself and felt it “suddenly melt away.” He said that a patient described the feeling as being “like a runner’s high” (a state that has been shown to involve the release of endogenous endorphins).

*Increase Pain,* the screen commanded, as the first run began. I tried to recall the mental strategies in which I had been prepped for increasing pain: *Dwell on how hopeless, depressed or lonely you felt when your pain was most severe. Sense that the pain is causing long-term damage.*

Dwelling on the hopeless loneliness of my pain certainly made the flames of my rACC spark. The mental image that I found increased my pain the most, however, was the one that matched the visual analogue of the rACC: *Picture a hot flame on your painful area. Try to make the flame grow in the painful area, and imagine it actually burning your flesh.*

Having recently read Ariel Glucklich’s extraordinary “Sacred Pain,” I had plenty of details of the burning of heretics and witches available to me. I had only to imagine the smell of sizzling hair to make the flames of my rACC explode.

*Decrease Pain,* the screen commanded.

The suggested pain-reduction strategies, however, did little to quell the flames on the screen. I pictured suffocating the pain with banal positive imagery: *flowing water or honey, something soft and gentle,* but my mind kept slipping back to the progress of the auto-da-fé, and the rACC fire flared.

Feel that sensation, but tell yourself that it is just a completely harmless, short-term tactile sensation.

Pilgrims and devotees all around the world choose to inflict pain upon themselves during sacred rites — from being nailed to crosses to dangling from hooks. For them, pain is an occasion for euphoria, not dysphoria. There are many historical records of the equanimity saints and martyrs often possessed during torture. The second-century Jewish martyr Rabbi Akiva, for example, continued to recite a prayer with a smile on his lips while the flesh was being combed from his bones. “All my life,” he explained to the puzzled Roman general orchestrating his execution, “when I said the words ‘You shall love the Lord your God with all your heart, and with all your soul, and with all your might,’ I was saddened, for I thought, When shall I be able to fulfill this command? Now that I am giving my life and my resolution remains firm, should I not smile?”

As Glucklich writes, the conviction that pain is a spiritual opportunity seems paradoxically anesthetizing — or, as a scientist would say, religious states of conviction can robustly activate the pain-modulatory system.

During my next Decrease Pain interval, instead of trying to picture a vacation, I imagined myself as a martyr, lucidly reciting *Though I walk through the valley of the shadow of death while being burned at the stake.*

My rACC activation — I noted — respectfully quieted. Then I remembered that the 23rd Psalm seems to have Christian associations, and since I was presumably being tortured for being half-Jewish, a Jewish prayer might be more appropriate. Unless, that is, I was being accused of witchcraft, in which case, I might be generally disillusioned with Judeo-Christian prayer. As I tried to settle on a fantasy, I noticed that my rACC stayed low: Irene Tracey’s theory of the modulating effects of distraction. By the last run, I had the strategies down — heretic-martyr: rACC down; heretic-victim: rACC up.

The results of the scan, Mackey showed me, revealed significant brain...
control. A week later, I was scanned again, this time in the offices of Omneuron. I could feel that it was easier to control my rACC with less reliance on elaborate fantasy; I was interacting more directly with my brain.

This learning effect was clearly seen in the recent Stanford study (which was financed in part by the National Institutes of Health). The first phase of the study looked at 12 subjects with chronic pain and 36 healthy subjects. (The healthy participants were subjected to a painful heat stimulus in the scanner and tried to modulate their responses. The chronic-pain patients, however, simply worked to reduce their own pain.) The chronic-pain patients who underwent neuroimaging training reported an average decrease of 64 percent in pain rating by the end of the study. (Healthy subjects also reported a significant increase in their ability to control the pain.)

“One big concern we had,” Mackey says, “is, Were we creating the world’s most expensive placebo?” To ensure against that, Mackey trained a control group in pain-reduction techniques without using the scanner (as in his previous study) to see if that was as effective as employing a $2 million machine. Mackey also tried scanning subjects without showing them their brain images or tricking subjects by feeding them images of irrelevant parts of the brain or feeding them someone else’s brain images. “None of these worked,” Mackey says, “or worked nearly as well.” Traditional biofeedback also compared unfavorably; changes in pain ratings of subjects in the experimental group were three times as large as in the biofeedback control group.

The second phase of the study, which is now under way, is designed to assess whether neuroimaging therapy offers long-term practical benefits to a larger group of chronic-pain patients. After the six sessions designed to teach them to regulate their pain, they will be observed for at least six months. The idea is to see whether they can fundamentally change their modulation system so that it can reduce pain all the time without constantly and consciously thinking about it. If so, the technique would not simply provide shelter from the storm of pain; it would bring about climate change.

“I believe the technique may make lasting changes because the brain is a machine designed to learn,” deCharms says. The brain is soft-wired (plastic) rather than hard-wired: whenever you learn something new, new neural connections are believed to form and old, unused ones to wither away. (Researchers refer to this as activity-dependent neuroplasticity.) In other words, if you actively engage a certain brain region, you can alter it.

Many diseases of the central nervous system involve inappropriate levels of activation in particular brain regions that change the way they operate (negative neuroplasticity). Some regions experience atrophy, while other regions become hyperactive. (For example, epilepsy involves hyperactivity of cells; stroke, Parkinson’s and other diseases involve the atrophy of nerve cells.) With chronic pain, it is believed that additional nerve cells, recruited for transmitting pain, create more pain pathways in the nervous system, while nerve cells that normally inhibit or slow the signaling, decrease or change function.

In addition, chronic pain results in a significant loss of other kinds of brain cells. A. Vania Apkarian at Northwestern University found that while the brain of a healthy person shrinks 2.5 percent a year, in a person with chronic back pain, it shrinks an additional 1.3 percent annually in the areas that involve rational thinking. I know chronic pain interferes with my concentration at times, but I never imagined that it could be truly impairing it! The Stanford technique may mitigate this harm by teaching people how to increase the efficacy of the healthy cells.

Moreover, the technique may offer a particular advantage over drug therapy. It is very difficult to design drugs to fix a problem in a specific region of the brain because the receptors that drugs target, like the opiate receptors, generally appear in multiple systems throughout the brain (which is partly why drugs almost always have side-effects). Neuroimaging therapy, on the other hand, is designed to teach control of a localized brain region.

“The technique gives people a tool they didn’t know they had,” Mackey says, “cognitive control over neuroplasticity. We don’t fully understand how this feedback mechanism is working, but it provides tangible evidence that people can change something in their own brains, which can be very empowering. It takes Buddhist monks 30 years of sitting on a mountain learning to control their brains through meditation — we’re trying to jump-start that process.” As to how exactly it works — how the decision-making parts of the brain (the prefrontal regions of the cortex) cause the change in the rACC — “Heck if I know!” he says. “How do we get the brain to do anything? We can map out the anatomical circuits involved and the general functions of those circuits, but we can’t tell you the mechanism by which any cognitive decision is translated into action.”

If neuroimaging therapy could treat pain, could it rewire the brain to fix other diseases, like depression, stroke and learning disabilities, or exercise the brain in ways that would make it cleverer and more adept at certain skills? Neuroimaging has shown, for example, that the part of the brains of London cabdrivers that regulates spatial relations is larger than usual and that learning to juggle creates visible changes in parts of the brain involved with motor coordination during three months of training. I’m constantly getting lost and dropping things. Could I exercise and strengthen those areas more quickly by, say, thinking about maps in the scanner by driving around London?

“What is the limit to neuroimaging therapy?” deCharms muses. “Could you learn to target the reward or serotonin system and up-regulate happiness? Could you augment psychotherapy by allowing the patient and the therapist to watch the brain?” — an idea Omneuron is already exploring, by bringing therapists and patients to the scanner and imaging patients’ brains as they undergo the sessions. “After all, talk therapy is about learning to understand thought processes — to understand neural substrates and change them,” he says.

HOW DEEP CAN the insights that functional imaging might offer really go?

What I’d like to do most is not fix problems or improve skills but use imaging as a vehicle for self-transparency. Instead of puzzling about my motivations, I’d like to be able to read my mind completely, like a book: for imaging to be the Plexiglas window through which I could finally see the ghost.

“Hmmm,” Dr. Scott Fishman, chief of the pain-medicine division at the University of California, Davis, said dubiously when I brought up this notion. “I’m not sure that functional imaging is actually looking at the mind. The mind is like a virtual organ — it doesn’t have a physical address that we know about. Functional imaging provides a two-dimensional snapshot of a three-dimensional or a four-dimensional event of this entity of the mind. Right now, imaging is just looking at the brain; we have to be honest about that.” Imaging shows the level of activation of different parts of the brain, from which we can extrapolate something about the mind, he points out, “but what we really need to see is how the parts talk to each other — and the complex nuances of their language.”

The brain has more than a hundred billion neurons. All functional imaging can tell us now is that a few hundred million of them in various areas become more active at certain times. It’s as if you were trying to conduct a symphony by watching a silent film of the concert. You would see the players in the bass section active at one moment, vigorously gesturing, and then the rest of the orchestra would join in, but you couldn’t hear the notes or how they form strands of melody and harmony and meld together to create the ethereal experience.

“Consciousness is not neurons firing — consciousness is a transcendent emergent phenomenon that depends on the firing of neurons,” says Dr. Daniel Carr, an eminent pain researcher who is now the C.E.O. of Javelin Pharmaceuticals. “The gears of a watch rotate and keep time, but the turning of the gears is not time. The question is, Is neuroimaging a picture of the experience of consciousness or is it a picture of a mechanism associated with that experience? Can there actually be a picture of an experience? Does a picture of a funeral or a wedding show you experiences? Or is there an unbridgeable gap there because you need to already understand the experience in order to interpret the photos? If a higher being told us how consciousness works, could we understand the explanation?”