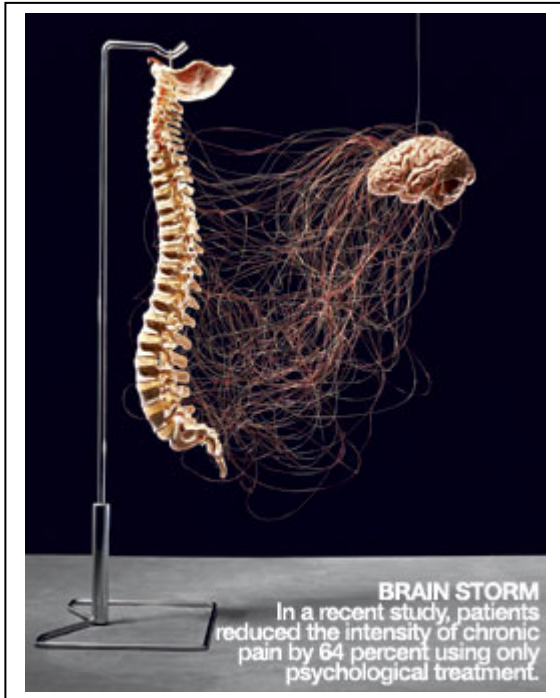


Chronic Back Pain is a Disease of the Nervous System, Not the Spine

Back pain strikes nearly 80 percent of all adults, yet its causes are not fully understood. A growing cadre of doctors and scientists now believes that chronic back pain is a disease of the nervous system, not the spine. This breakthrough has opened the doors to new kinds of treatments that could banish back pain forever.



By: Jonah Lehrer; Photographs: Craig Cutler [Updated: Oct 31, 2008 - 6:22:28 PM]

In its darkest moods, the demon lurking in Marc Sopher's back made it almost impossible for the family doctor to carry on with his daily routine. It would pound his lower back, sending dull throbs of pain up his spine, and then fire sharp bolts of pain down one leg and then the other. At first, Dr. Sopher tried to ignore the pain. He assumed that he'd strained something in his spine, perhaps herniated a disk or pinched a nerve. "I'm a traditionally trained physician," he says. "I started taking some anti-inflammatories and I waited for my back to heal." But the demon wouldn't go away. When holding meetings, he'd have to stand up and stretch his back. When driving, he'd have to stop and get out of the car to ease the tension in his spine. When reading bedtime stories to his kids, he'd have to lie on his stomach. There was no anatomical explanation for the extremity of his pain. "I tried to soldier on the best I could," he says. "I honestly believed I'd be living with pain for the rest of my life."

The majority of people with back pain (estimates run as high as 90 percent) will get better within seven weeks with little or no medical treatment. The body heals itself, the inflammation subsides, and the nerve relaxes. These people go back to work, pledging to avoid the sort of physical - triggers that caused the pain in the first place. About 10 percent of patients don't get better. Their pain gets worse and worse: It is chronic. One day, these people find themselves lying supine on the floor, wondering what they did to deserve such agony.

Today, Dr. Sopher, who lives in Exeter, New Hampshire, no longer has back pain. He has slain his demon. When I meet him, he's drenched in sweat, having just run eight miles and played a game of tennis. Later, he'll ride his bike. His short hair is salted with white—Dr. Sopher is 46—and he still has the taut body of a young athlete. But Dr. Sopher wasn't healed by conventional medicine. He didn't undergo surgery or get epidural injections or take painkillers. Instead, Dr. Sopher is one of the thousands of patients suffering from chronic back pain who got better by treating his mind.

He learned to think differently about his pain, and that's when his pain went away. This narrative might sound suspicious—there's no shortage of phony treatments for chronic back pain—but a growing body of scientific evidence supports it. Chronic back pain is now predominantly seen as a disease of the nervous system, not the spine. It's a problem suited for psychologists and neuroscientists, not surgeons. The best treatments are often the least invasive.

America is in the midst of a back-pain epidemic. The numbers are staggering: There's an 80 percent chance that, at some point in your life, you'll suffer from severe back pain. Treating back

pain costs about \$26 billion annually and it currently accounts for 2.5 percent of our country's total health-care spending. If worker compensation and disability payments were taken into account, the cost would be even higher.

The conventional medical treatment for back pain follows a predictable script. After the patient is interviewed and given a physical exam, he or she undergoes a series of diagnostic tests. This normally includes x-rays, CT scans, and MRIs. The end result is an astonishing array of detailed anatomical pictures. Doctors no longer need to imagine the layers of tissue underneath the skin. Now they can see everything.

Unfortunately, all this seeing has limited results. After undergoing the full range of diagnostic tests, 85 percent of patients suffering from lower-back pain still don't receive a precise diagnosis. The pain can't be pinpointed; there are just too many moving parts. Instead, their suffering is parceled into a vague category, such as lumbar strain or spinal instability. But even when a patient is given a specific structural diagnosis, it's not clear how meaningful the diagnosis actually is. Look, for example, at herniated disks, one of the most common "causes" of back pain. A 1994 study published in *The New England Journal of Medicine* imaged the spinal regions of 98 people with no back pain or back-related problems. The pictures were then sent to doctors who didn't know that the patients were not in pain. The end result was disturbing: Eighty percent of the pain-free patients exhibited "serious problems" such as bulging, protruding, or herniated disks. In 38 percent of patients, the MRIs revealed multiple damaged disks. The disconnect between "disk degeneration" and back pain increases with age: More than 80 percent of people over the age of 60 who don't have any back pain still demonstrate significant disk degeneration. These structural spinal abnormalities are often used to justify expensive treatments like surgery, and yet nobody would advocate surgery for people without pain. In the latest clinical guidelines issued by the American College of Physicians and the American Pain Society, doctors were strongly recommended not to "obtain imaging or other diagnostic tests in patients with nonspecific low back pain." In too many cases, the expensive tests proved worse than useless.

The Mind-Body Prophet

Dr. Sopher banished his demon by reading a book. It was *Healing Back Pain*, by John Sarno, MD, a physician at New York University. "Once I started reading," says Dr. Sopher, "I couldn't stop. It was like a revelation. As the hours went by, I became aware that I'd been sitting for a long time without any pain." While nothing had changed in Dr. Sopher's back, he was learning how to think about his pain in a new way. "That's when I reminded myself that I'm a serious doctor, and just reading a book isn't supposed to cure pain. That's when I decided to contact Dr. Sarno. I needed to learn how this was done."

The Rusk Institute of Rehabilitation Medicine lies on the eastern edge of Manhattan. It's a squat brick building overlooking a highway. Watching patients enter the institute is a sobering experience. The full variety of human limps and gimps is on display. People hobble through the doors wearing cervical collars and shoulder slings and elaborate knee braces. They lean on canes and crutches. It's a slow-moving parade of pain.

Dr. Sarno is 84 years old—he has been practicing medicine since 1950—but he still sees new patients three days a week. He talks slowly, with the pedantic patience of someone used to explaining his ideas. "When I first started treating patients with back pain," says Dr. Sarno, "I practiced conventional medicine. I relied on all the usual tools, like injections and strengthening exercises. As the years passed, I grew very frustrated because I realized that all the conventional

treatments were utterly useless. My patients weren't getting better."

Dr. Sarno's failure caused him to question a fundamental assumption of modern medicine. In general, doctors assume that bodily pain is a response to bodily injury. Our back hurts because a disk is herniated or a muscle is strained. The pain is due to a structural abnormality. Fix the abnormality and the pain goes away.

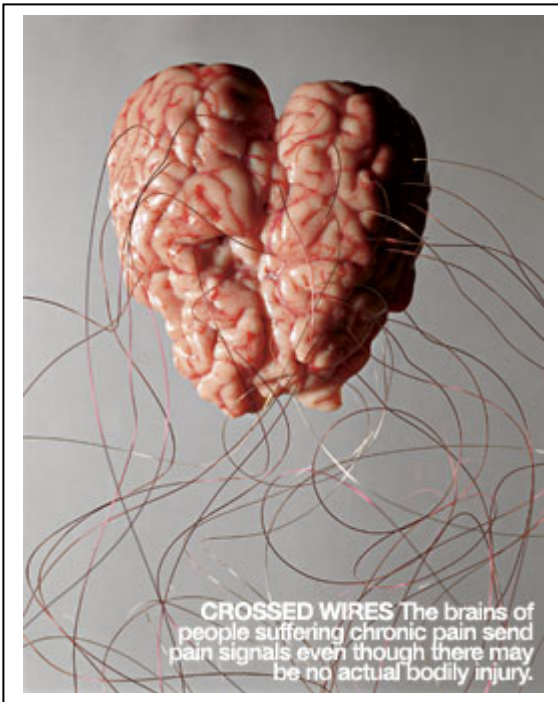
But Dr. Sarno began to doubt this explanation, at least when it came to chronic back pain. "Once I started thinking about it," he says, "the structural diagnosis stopped making sense. It couldn't explain a whole range of issues, like why these chronic-pain patients never got better, or why they also suffered from a range of other illnesses." Many of Dr. Sarno's patients continued to experience debilitating pain even after their structural problems were "fixed." What, then, was causing the chronic pain? If nothing was wrong with the body, then where did the pain come from? Why were healthy people hurting? That's when Dr. Sarno had his epiphany: Chronic back pain is caused by the mind.

This theory, which Dr. Sarno has expounded in a series of popular books that have sold more than 750,000 copies, has an alluring simplicity. He argues that much of our physical suffering is rooted in the machinations of the unconscious mind. Sometimes, when we repress our anger, deal with undue amounts of stress, or experience some upsetting emotion, the mind induces bodily pain as a form of distraction. It turns a minor physical incident—like lifting a heavy object—into a set of debilitating physical symptoms. Our back hurts so that we don't think about or feel our emotional hurt. The pain, of course, is yet another source of stress, which makes the suffering worse. The pain becomes a downward spiral. The only way to "cure" chronic back pain (what he calls tension myositis syndrome, or TMS), according to Dr. Sarno, is with rigorous psychological treatment. Patients learn to remind themselves that the pain, though real, is rooted in their own minds. Unless the patient unconditionally accepts Dr. Sarno's diagnosis, he won't get better. It is the faith that sets him free.

Dr. Sarno's ability to make chronic pain disappear shouldn't be dismissed as just another instance of the placebo effect. While there have been no independent studies of his success rate, the anecdotal evidence is certainly suggestive. An investigative story by ABC News randomly selected 20 former patients from Dr. Sarno's files and tracked them down: All 20 reported they were "better" or "much better." Entering one of the numerous forums dedicated to Dr. Sarno on the Internet is like wandering into a Pentecostal revival meeting. New testimonials appear every day, with people confessing that years of chronic pain ended as soon as they read one of Dr. Sarno's books. They tell stories of expensive surgeries that didn't help and scary spinal diagnoses that couldn't be treated. And then, after years of suffering, they stumbled upon Dr. Sarno and they were saved.

Dr. Sarno is convinced that he has discovered something important about chronic back pain. As he puts it, "The most powerful scientific proof of the diagnosis is that the majority of my patients get better, despite the existing structural abnormalities." But there is little scientific evidence for Dr. Sarno's theories; he hasn't published a medical paper in years and the medical establishment doesn't recognize TMS. Dr. Sarno's notions of the unconscious mind are largely derived from Freud, and Freud isn't exactly cutting-edge science. One back-pain specialist told me that, while he was sympathetic to Dr. Sarno's "psychological theme," he was troubled by his "penchant for constructing theories without the necessary foundation of facts." In other words, Dr. Sarno could well be right, but for the wrong reasons.

The Science of Pain



All pain hurts, but from the perspective of the brain, there are two distinct types. The first type of pain is sensory. When we stub our toe, pain receptors in the foot instantly react to the injury and send an angry message to the somatosensory cortex, the part of the brain that deals with the body. This is the type of acute pain that doctors are trained to treat. The hurt has a clear bodily cause: If you inject an anesthetic such as novocaine into the stubbed toe, the pain will quickly disappear.

The second pain pathway is a much more recent scientific discovery. It runs parallel to the sensory pathway, but isn't necessarily rooted in signals from the body. The breakthrough came when neurologists discovered a group of people who, after a brain injury, were no longer bothered by pain. They still felt the pain and could accurately describe its location and intensity, but didn't seem to mind it at all. The agony wasn't agonizing.

This strange condition—known as pain asymbolia—results from damage to a specific subset of brain areas that are involved in the processing of emotions. As a result, these people are missing the negative feelings that normally accompany painful sensations. Their muted response to bodily injury shows that it is our feelings about pain—and not the pain sensation itself—that make the experience of pain so awful. Take away the emotion and a stubbed toe isn't so bad.

Chronic pain is the opposite of pain asymbolia. It's what happens when the brain can't stop generating the negative emotions associated with painful sensations. These emotions can persist even in the absence of a painful stimulus, so we feel an injury that isn't there. It's like feeling the pain of a stubbed toe forever. Doctors have traditionally focused on the bodily aspects of chronic pain. They assume that a healed body is a painless body. If a patient has chronic back pain, then he is typically prescribed painkillers and surgery so that the pain signals coming from his spinal nerves are stopped. But the dual pathways of pain mean that this approach treats only half of the pain equation. Unless you find a way to treat the emotional pathway, then the chronic pain will continue.

"The standard model of pain—the same model that is still taught in every medical school—is that you treat the pain by fixing the underlying pathology," says Sean Mackey, MD, PhD, an associate professor at Stanford University and director of the pain management division. But the reality of pain, says Dr. Mackey, is much more complicated. "We're now beginning to recognize that you can't talk about chronic pain without talking about its psychological aspects. It's a condition in which signals from the body are literally distorted by the brain."

Dr. Mackey is at the forefront of a new paradigm in pain research. In many respects, he is an unlikely revolutionary. "My PhD is in electrical engineering," says Dr. Mackey. "Nobody was more mechanistic than I was. When I began treating patients, I was very interested in trying to identify the structural source of the pain. I'd do lots of injections. But what I found, much to my surprise, was that my patients were getting better more from my talking with them than from any medical procedure. That intrigued me, and so I started to look into the mechanisms of why talking to my patients might reduce their pain. That's what led me to study the brain and not just the body."

Dr. Mackey's personal experience now has strong scientific support. In recent years, the medical establishment has started to realize that one of the most powerful ways to treat chronic back pain—or any pain—is by treating the mind. When patients are taught how to deal more effectively with the negative emotions that accompany chronic pain, they often experience dramatic improvements. The pain that wouldn't disappear is suddenly diminished. Psychological interventions can heal the hurt.

Robert Kerns, PhD, has been studying the psychology of pain for 30 years. He's an associate professor of psychiatry at Yale University and the national program director for pain management at the Veterans Health Administration. When Kerns was in graduate school in the late 1970s, he treated a patient with terrible back pain as a result of kidney disease. Even though this patient had a serious physical condition, Kerns noticed that psychological therapy helped her cope with the pain. "That's when I realized that a person's thinking could affect his or her pain experience," he says. "Chronic pain isn't beyond our control."

At the time, there was little hard evidence to support such mental interventions. Treating chronic pain with psychological therapy was like treating cancer with a poem: The best thing most doctors could say about it was that it would do no harm, but few expected it to actually help. Pain, after all, was a medical condition. Therapy was just words. But the words are working. Kerns's most recent study, published in January 2007 in *Health Psychology*, is also his most definitive. It's a meta-analysis of 22 trials that looked at the effectiveness of psychological treatments for patients with chronic lower-back pain. The statistics were complicated, but the results were clear: Psychological treatments made the pain go away. Patients with chronic back pain could reduce their suffering by learning how to think differently about their pain. Benson Hoffman, PhD, an associate professor at Duke University and first author on the study, was surprised by the robustness of the data. "Going into the study," says Hoffman, "I thought that psychological interventions would probably increase the patients' quality of life, but not actually reduce their pain. But my hypothesis was wrong. These psychological treatments reduced the pain more than anything else did."

Think for a moment about what this means: These patients received routine medical care that failed to provide substantial relief. And yet, after just a few psychological treatment sessions, their pain started to subside. According to the meta-analysis, the two particularly effective psychological interventions were cognitive behavioral therapy and "self-regulatory therapies" such as biofeedback. Cognitive behavioral therapy is a popular form of talk therapy that teaches patients how to adopt a problem-solving approach to their pain. The simple premise of the treatment is that we are capable of controlling our own thoughts, emotions, and experiences. Therapists teach patients specific mental exercises, such as keeping a journal or practicing relaxation techniques, that help them manage their negative feelings and alleviate their suffering. Self-regulatory therapies show people how to take back control of their bodies. By giving patients information about their own internal processes (e.g., readouts of their blood pressure and brain waves), the therapy teaches them how to modulate these processes. The mind needn't be a slave to the flesh.

"Many patients with chronic back pain develop a sense of hopelessness," says Kerns. "These therapies show them that they can develop everyday strategies that make them feel better. I think one of the things that modern medicine has forgotten is that it's important to treat the whole person, and this means addressing both the physical and psychological aspects of the pain. When it comes to back pain, just fixing a 'broken' body part often isn't enough."

One of the first studies to demonstrate the importance of psychological factors for back pain came

from an investigation of 3,020 employees at Boeing in the 1980s. Over a four-year period, about 10 percent of these employees reported chronic back pain. When doctors analyzed the factors that predicted the onset of this pain, they were surprised to learn that structural back problems played a negligible role. Factory workers who often lifted heavy objects were no more likely to experience disabling pain than office workers. Instead, the best predictor of chronic pain was emotional distress: Employees suffering from depression or stress were much more likely to suffer from back pain.

A study more recently published in *Spine* made a similar point. Eugene Carragee, MD, a professor and vice chairman of orthopedic surgery at Stanford University School of Medicine, was the lead author. He tracked nearly 200 patients over five years, attempting to better understand the specific structural ailments that cause chronic back pain. The researchers imaged people in MRI machines and used discographies to assess the possible structural sources of back pain. They also conducted regular psychological evaluations.

Dr. Carragee's results, like earlier studies, showed that neither discographies nor MRIs were reliable predictors of severe back pain. While two-thirds of patients with chronic pain had small cracks in their disks, so did 24 percent of patients with no pain at all. "The real issue," he says, "is, Why do some people have a mild backache and some have crippling pain?"

To answer this question, Dr. Carragee analyzed the psychological evaluations of his patients. He soon discovered that a person's emotional state—and not the anatomical state of his back—was the best predictor of back pain. As Dr. Carragee notes, "The structural problems were really overwhelmed by the psychosocial factors. Almost without exception, people without any of these mental or social risk factors were able to deal with their backache. But people with a psychological problem had a much tougher time doing that. For them, the pain was often crippling and catastrophic."

While scientists have yet to find the specific mechanisms that connect psychological problems to chronic pain, they are uncovering some clues. One possibility is that mental disorders make people more vulnerable by weakening the brain regions and neurotransmitter systems that are involved in the perception of chronic pain. For example, a brain-imaging study published last August by researchers at the University of Wisconsin at Madison found that people with clinical depression were much less able to regulate their negative emotions. According to Tom Johnstone, PhD, who led the research, when depressed individuals tried to turn off their emotions, these attempts backfired. The more effort they put in, the more activation there was in the emotional areas of the brain. As a result, bad feelings tended to spiral out of control.

A similar process might be at work in chronic pain. According to this hypothesis, pain persists in the emotional areas of the brain because patients are unable to turn it off. Whenever they think about the pain, they just make it worse. The Wisconsin researchers speculate that depressed individuals might have a "broken link" in the brain, which makes the regulation of negative emotion impossible. What makes this research valuable is that it opens up new possibilities for treating chronic pain. In recent years, for example, doctors have found that antidepressants, especially tricyclics, are often effective treatments for chronic back pain. These drugs help control the emotions that the patients cannot.

Stress is another risk factor for chronic pain. One back surgeon, who wished to remain anonymous for fear of offending his patients, says he has seen several men develop back pain shortly after becoming engaged. "Weddings are stressors," he says, "and that stress can exacerbate the

experience of pain.” Intriguing clues are beginning to emerge as to how stress might modulate pain. Joyce DeLeo, PhD, a neuroscientist at Dartmouth Medical School, has discovered that chronic pain is often triggered by a response from the immune system. When DeLeo used mice that were missing a specific type of immune receptor, the mice proved less vulnerable to pain’s lingering effects. Of course, it has long been recognized that bouts of stress can profoundly alter the nature of immune response. “There are many psychological and social variables that can amplify the experience of pain,” says Dr. Carragee. “You can’t just wield a scalpel and make it go away.”

Mind Over Matter

The moral of these studies is clear: To fix chronic back pain, doctors have to look above the neck. Just as MRI and CT scans have enhanced doctors’ understanding of the spine (albeit not in the perfect way they had anticipated), powerful new brain-imaging tools are shedding light on how chronic pain affects both the structure and function of the mind and offering a glimpse of future treatments.

Imagine you are a patient with serious back pain, and when you walk into your doctor’s office, instead of doing the usual physical exam and patient interview, he tells you he is going to study your mind by using an fMRI (functional magnetic resonance imaging) machine, which measures brain activity. He barely glances at your back. By simply examining a few variables inside your head—the size of certain brain regions, the concentration of certain brain chemicals—he would be able to predict about 80 percent of the individual variance associated with your chronic back pain. In other words, he’d have a rather accurate sense of how intense your pain is and how long you’ve been suffering. He would recommend treatments that block or compete with the patterns of brain activity associated with chronic pain or recommend psychological therapy. In contrast, the conventional method of diagnosis, which involves studying the spine, can explain only about 25 percent of patients with back pain. When it comes to diagnosing chronic back pain, the brain reveals more than the body.

A. Vania Apkarian, PhD, is a professor of neuroscience at Northwestern University. He has been studying the neural underpinnings of chronic pain for more than 20 years. In 2004, he published a paper demonstrating that chronic back pain appears to cause brain damage. For each year of agony, people lose about a cubed centimeter of gray matter. With time, it adds up: Apkarian found that subjects with chronic back pain had anywhere from 5 percent to 11 percent less gray matter than control subjects. The suffering is literally toxic.

In a 2006 paper published in *The Journal of Neuroscience*, Apkarian’s lab located the specific brain areas triggered by chronic back pain. The scientists found that chronic pain—unlike acute pain—activated brain regions typically associated with negative emotions, thus providing further evidence that chronic pain is really an emotional disorder. It’s a malfunction of the second pain pathway. “It’s as if people with chronic pain have internalized the pain,” says Apkarian. “It has become part of who they are. That’s why you can’t just treat the body.”

At first glance, this data is dispiriting. The pain of longtime sufferers appears to be literally built into their brains, cemented in their souls. But Apkarian is also working on treatments that might alleviate the suffering at its neural source. In November 2007, Apkarian’s lab published a paper in *Pain* that documents the ability of a drug called D-Cycloserine to end chronic pain in rats. While D-Cycloserine was originally designed to fight tuberculosis infections, it also appears to suppress the emotional component of chronic pain. After 30 days of pharmaceutical treatment, the rats seemed

to have a large reduction in pain behavior. Apkarian is hoping to begin a clinical trial with chronic-back-pain patients later this year. “When we do this in a clinical trial, we expect people to say, ‘I still have the pain, but it’s not bothering me anymore,’ ” says Apkarian. “We think they will have a physical awareness of the pain, but its emotional consequences will have decreased.” The chronic part of chronic pain will have been erased from the brain.

Despite the persuasive body of evidence demonstrating the psychological component of chronic back pain, the vast majority of patients still reject any diagnosis that smacks of psychology. Dr. Sarno holds the medical establishment responsible for this state of affairs. “What’s going on now is a disgrace,” he says. “You have well-meaning doctors making structural diagnoses despite a serious lack of evidence that these abnormalities are really causing the chronic pain. All these incorrect diagnoses actually make it difficult for the patients to benefit from mind-body diagnoses.”

Everyone agrees that a big part of the solution is better patient education. “A lot of what I do is educate people about what their MRIs are showing and how it relates to their back pain,” says Dr. Mackey. “I remind them that only young people have spines that look perfectly healthy. Degeneration is often part of a normal process and it doesn’t necessarily imply that their pain is a result of these changes. Patients have to get beyond their fear of pain, because the fear keeps them from progressing. It’s like they slip into a state of learned helplessness.”

Many patients also find the possibility of a psychological diagnosis insulting. They assume that if the pain has a mental component, then it must be make-believe. It’s an issue Dr. Sopher dealt with himself, and that he now deals with when treating his patients. “When you tell a patient that his mind might be responsible for his pain, he thinks you’re calling him crazy,” he says. “I always tell patients that the pain is no less real because it’s being caused by the mind. It just means that getting better means changing something in your mind, not your back.”

The good news is that while we can’t always realign our spines or fix our ruptured disks, we can control our perception of chronic pain. With the proper training, we can alleviate our own suffering. That, at least, is the optimistic conclusion of a recent Stanford study performed by Dr. Mackey and other researchers. The study used real-time fMRI brain imaging to teach people with chronic pain how to modulate their conscious response to the pain. Some of the subjects distracted themselves with pleasant thoughts, while others recited mantras or listened to soothing music. Despite the diversity of strategies, each of the patients could see the direct impact of his palliative thoughts. They watched as the specific parts of their brains associated with chronic pain gradually subsided in activity. They had become their own painkillers.

The results of the experiment were dramatic. Most of the chronic-pain patients reported a decrease in pain intensity, with an average decrease of 64 percent. The patients had stopped being the helpless victims of a structural abnormality in the body and could now focus on dealing with the pain in their minds. Simply knowing that they could control the pain made the pain less terrible.

Christopher deCharms, PhD, a lead author on Dr. Mackey’s paper, is trying to take this therapeutic approach mainstream. He has started a company called Omneuron, which makes the experimental treatment available to a wider audience. A standard session goes like this: A patient lies in a brain scanner while experiencing pain, and he watches as his brain flares up in agony. He sees the smear of neural activity that makes him suffer. Then, with the help of a trained therapist, the patient learns how to consciously turn off the specific brain areas that correlate with the chronic pain. After a few sessions, the awful symptoms begin to fade away. The pain is no longer permanent. It’s a real-world example of mind over matter.

The Brain in Chronic Pain By Emily Singer

Sophisticated brain-imaging studies suggest new ways to treat chronic pain.

Pain relief: Imaging studies have identified brain areas gone awry in people with chronic pain.



Anyone who suffers from chronic pain knows that the experience is fundamentally different from enduring a scratch or a broken toe. Growing evidence from brain-imaging studies supports this notion: people with chronic pain show fundamental differences in both the structure and function of their brain. Scientists are now using these findings to develop and test new drugs created specifically for chronic pain.

"It should eventually be possible to identify patterns of brain activity involved in perpetuating chronic pain, and then to introduce interventions that we know from published evidence can block or compete with those patterns," says [Richard Chapman](#), director of the Pain Research Center at the [University of Utah](#), in Salt Lake City.

Chronic pain is one of the biggest medical health issues in the Western world; it costs the United States about \$150 billion a year. Unlike with acute pain, the causes of chronic pain are often unclear--for example, doctors can identify a physical source in only about 10 percent of those with chronic back pain. A growing number of studies suggest that chronic pain should be viewed as a progressive disease, likely triggered by aberrant but potentially permanent changes in the brain.

The painkillers that help headaches and broken bones do little for chronic pain, leaving a huge need for new treatments. But developing them has been difficult. Perception of pain depends strongly on our level of attention and our emotional state--two factors that are difficult to study in animal models. "We don't have one drug developed from preclinical models of pain that works for chronic pain," says [Irene Tracey](#), a scientist at the University of Oxford, in England, who studies pain.

Now scientists are aiming to develop and test new drugs using human brain imaging. [A. Vania Apkarian](#) and his colleagues at Northwestern University have found a series of abnormalities in the brains of chronic pain sufferers: the part of the prefrontal cortex linked to decision making appears to have shrunk in chronic pain patients. And another part of the prefrontal cortex linked to emotion is hyperactive. In fact, a unique study assessing background pain in chronic back-pain patients suggests that the constant pain these people experience is linked to activity almost entirely in emotion-regulating parts of the brain.

Researchers used functional magnetic resonance imaging (fMRI), which measures brain activity, to study background pain. They asked back-pain patients to continually rate their pain while lying in the scanner, and then the researchers compared brain activity patterns during periods of constant pain with those during periods of worsening pain.

While activity patterns during flare-ups resembled those previously linked to acute pain, the pattern associated with constant background pain was distinct: it centered on the medial prefrontal cortex,

a brain area involved in emotion and sense of self. "It almost seems like they've turned off the sensory part and are suffering entirely from the emotional aspect," Apkarian says.

Given these findings, the scientists are beginning human tests of a compound called d-cycloserine, an FDA-approved antibiotic that also blocks certain receptors in the brain. (It is currently being tested for treating post-traumatic stress disorder and other conditions.) "We think it increases transmission within the prefrontal cortex to better control the emotional component of pain," says Apkarian. "This will be the first hypothesis-driven test for a pain drug driven by human-imaging studies."

Another hot target for chronic pain is the modulatory [system](#) that humans have evolved to suppress pain when necessary--so that they can run from a predator while wounded, for example. Preliminary evidence suggests that chronic pain sufferers aren't good at recruiting this inhibitory system. Indeed, ongoing studies suggest that people with chronic pain may be hyperactive in the opposite direction: they amplify pain signals on their way to the brain. [Sean Mackey](#), a physician and researcher at Stanford [University](#), and his colleagues are now studying the brain stem and spinal cord, two crucial components of this modulatory system that have traditionally been very difficult to assess with fMRI. These parts of the nervous system move with every breath and heartbeat, so the researchers had to develop new analysis methods to generate clean images.

Identifying the neural signatures linked with chronic pain may also provide a new way to screen experimental drugs for human testing. A small study of pain patients given gabapentin--an epilepsy drug also used to treat nerve pain--showed significant activity changes in the parts of the brain that respond to pain. Drug developers could use this measure as a quick way to assess which experimental compounds to send for further testing, says Tracey, who is developing the technique. "We are getting to the point where we can test novel compounds."

In the absence of effective drugs, many chronic pain patients have turned to behavioral therapies to try to control their pain. Tracey's studies have shown that people who are better at distracting themselves from pain show more activity in a specific part of the pain modulating system. "Maybe we could use brain imaging as a screening tool to determine who would do well on cognitive behavioral therapy," she says.

One of the newest experimental approaches to controlling pain is real-time fMRI, in which patients watch their brain activity in real time as they try to consciously control brain areas involved in pain. (See "[Seeing Your Pain](#).") Mackey and his collaborators have shown that chronic pain patients could reduce their pain in the short term using this method--essentially, a more precisely targeted form of biofeedback--and the researchers are now assessing long-term effects. Mackey says that brain-imaging studies of these patients are shedding light on how people learn to control their pain, and which parts of the brain are the most effective targets.

Scientists don't yet know why some people develop chronic pain and others don't. "There seems to be cortical reorganization at a high level because of the injury itself, but whether that's a coping mechanism or just a consequence, we don't know," says Apkarian. "Some people might be predisposed to chronic pain. But it still seems to get worse as they live with the pain."

He and others say that one of the biggest benefits to brain-imaging studies of chronic pain is that they convince both patients and doctors that it really exists. "It's been revolutionary in providing

validation to people that pain is something with a real neurological basis," says Mackey. "We can point to areas of the brain and say, That's part of the brain that's dysfunctional."

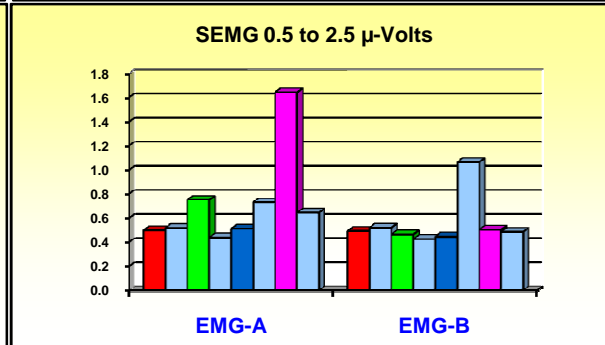
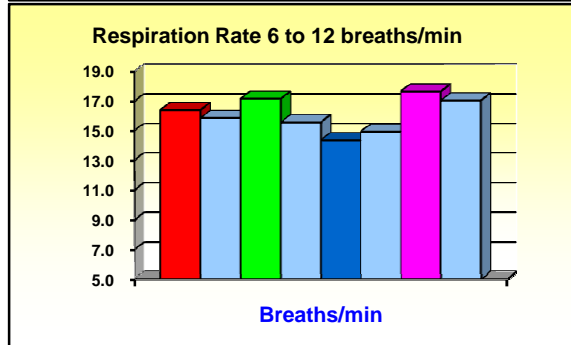
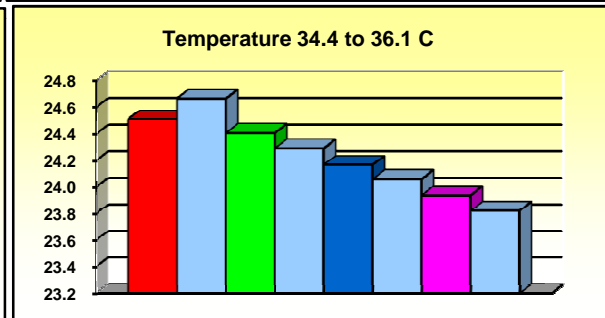
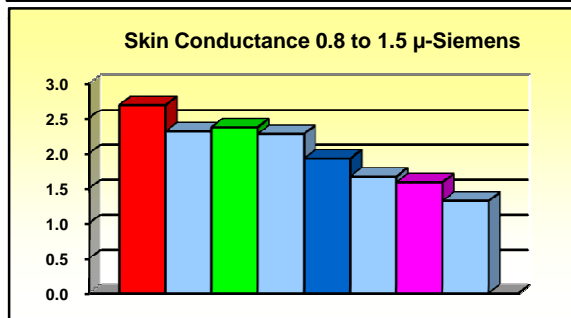
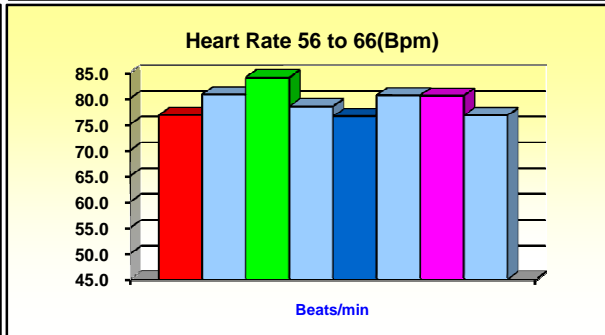
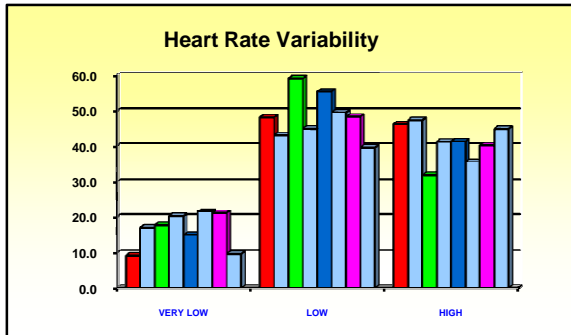
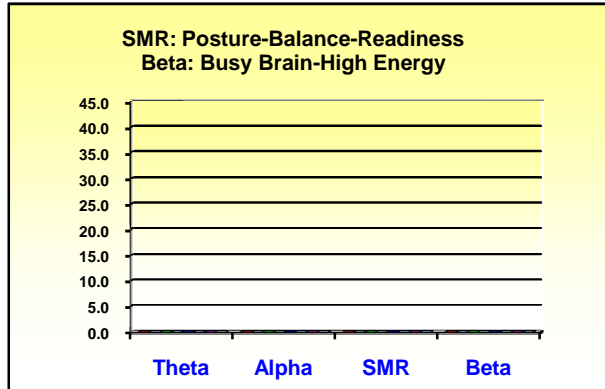
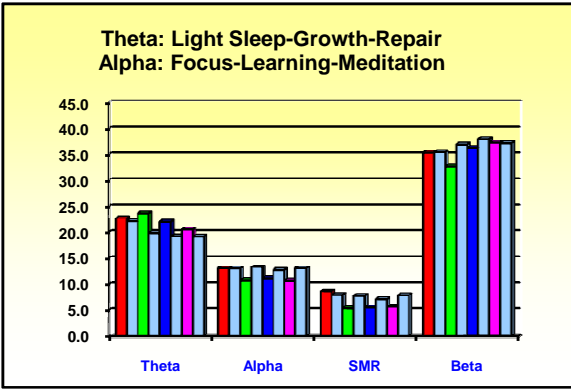
Credit: Technology Review -Thursday, November 15, 2007

(V-sio) Stress Report

Left

Percent Power of EEG

Right



Legend:

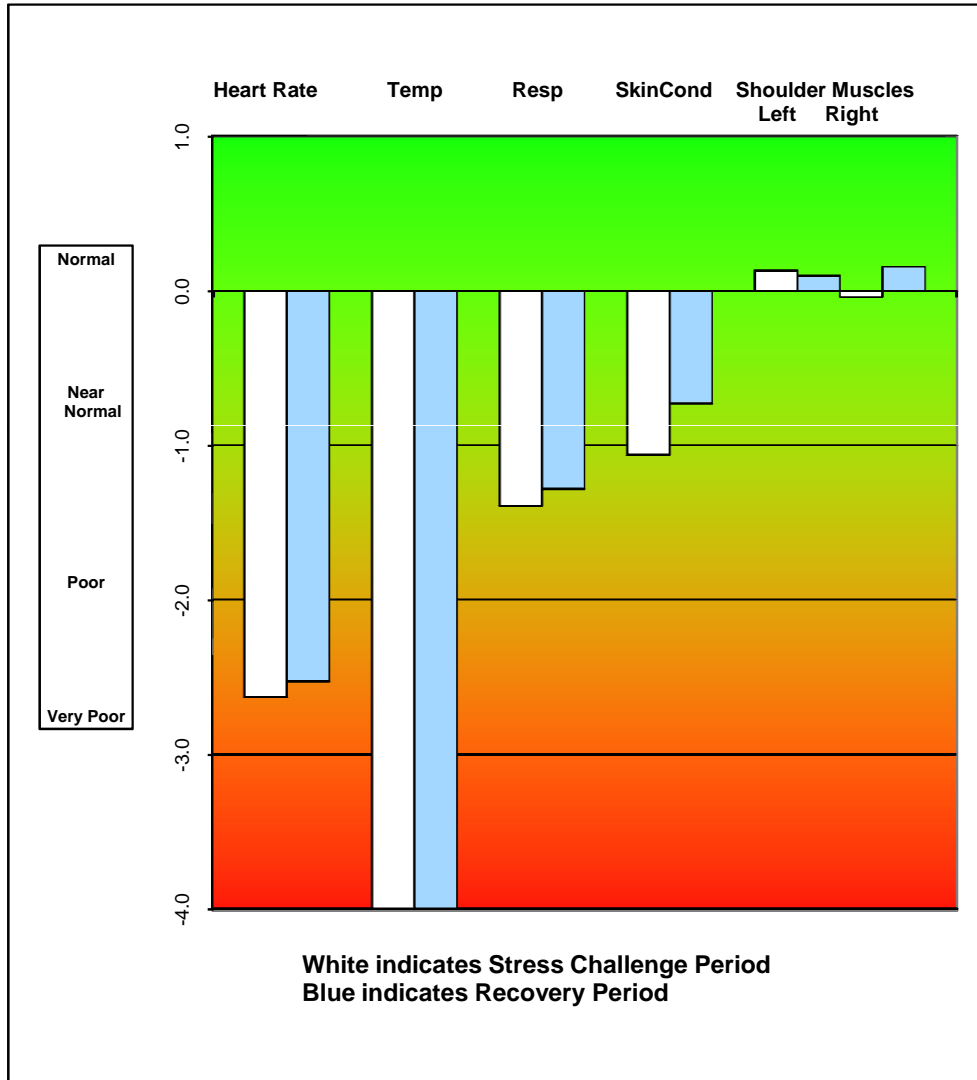
- Eyes Open BL
- Eyes Closed BL
- Math Test
- Recovery1
- Sounds
- Recovery2
- HRV Task
- Recovery3

SUBJECTIVE: INITIAL /10 FINAL /10

Patient Name: Client: S M

Session Date: 16/07/2008

Results Summary



Patient Name: Client: Simone Mortensen

Session Date: 16/07/2008



Stress

Can Be More Than a Pain in the Neck

Stress can have devastating effects on your health, your relationships, and even your performance at work. Yet the latest in medical research indicates that it is your response to stress that plays the critical role – not the stressors themselves.

To help you manage your response to the stress in your life, our office offers a cutting edge Stress Response Evaluation. This 12 to 15 minute, pain-free evaluation uses cutting edge technology to evaluate how your nervous system responds to stress. The results of this exam will help us identify problem areas and create a comprehensive plan for improving your stress response.

Using the same technology as world championship soccer teams, gold medallist Olympians, and space bound astronauts, we will help train your nervous system to better handle the stress in your life – giving you much more control over stress and limiting its damaging effects.

There are few things – if any – more important than your health, your relationships, or your job. Come in today for a quick evaluation so we can help you keep them . . . and keep them strong.

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