

Science is showing that how you feel isn't just about what you eat, or do, or think. **It's about what you believe.**

The pilgrim wasn't sure he'd make it to the Chapel of Grace. It was agony to walk at all, let alone endure the 70 miles that thousands of believers trek each year to behold an enshrined wood statue: the Black Madonna of Altötting.

Richard Mödl had recently broken his heel, but in 2003 he was determined to complete his first pilgrimage from Regensburg to Altötting, Germany. He figured if the pain got too bad he could always hitch a ride. But he had a deep faith in the Virgin Mary's ability to deliver him. So he walked. And walked. "When you are on your way to Altötting, you almost don't feel the pain," he says.

Today, at 74, Mödl has a warm smile and a wiry frame that looks as if it could survive a charging rhinoceros. Since the healing of his foot, he's made the pilgrimage 12 more times, and he's a passionate believer in its transformative power. Mödl is not alone in his belief. Whether it takes the form of a touch of the Holy Spirit at a Florida revival meeting or a dip in the water of the Ganges, the healing power of belief is all around us. Studies suggest that regular religious services may improve the immune system, decrease blood pressure, add years to our lives.

Religious faith is hardly the only kind of belief that has the ability to make us feel inexplicably better. Six thousand miles from Altötting, another man experienced what seemed to be a medical miracle.

Mike Pauletich first noticed he had a problem in 2004. His aim with a baseball was off, and his arm hurt. His hand shook a little, and, strangest of all, his wife noticed he never smiled anymore.

Mike Pauletich, during a trial at Stanford University, believed he had surgery to alleviate Parkinson's symptoms. In fact he'd received a sham surgery—but he did feel significant relief.

“Whether it was placebo or some effect of a drug,” he says, “it doesn't matter to me.”

Figuring he had carpal tunnel syndrome, he went to the doctor. But his bad aim wasn't because of his arm, and the reason he wasn't smiling wasn't because his arm hurt. At 42 years old, Pauletich had early onset Parkinson's disease. His doctor told him that within a decade he wouldn't be able to walk, stand, or feed himself. Pauletich didn't deteriorate as much as his doctor predicted, but for years he struggled with the disease and with depression, as talking and writing became ever harder. Then, in 2011, he turned to Ceregene, a company that was testing a new gene therapy. Parkinson's is the result of a chronic loss of the neurotransmitter dopamine. It had been shown in monkeys that injections of a protein called neurturin could halt the progress of the disease by protecting and possibly repairing damaged dopamine-secreting neurons. Ceregene's experi-

mental treatment was to cut two holes, one in each hemisphere of the brain, through a patient's skull and inject the drug directly into the target regions.

Pauletich's improvement after the surgery was impressive. Before the trial he had struggled to move around. He had to constantly explain to clients of his technology development company that his slurred speech wasn't caused by drinking. After the procedure his shaking disappeared, his mobility improved, and his speech became markedly clearer. (Today you can hardly tell he has the disease at all.) His doctor on the study, Kathleen Poston, was astonished. Strictly speaking, Parkinson's had never been reversed in humans; the best one could hope for was a slowdown in the progression of the disease, and even that was extremely rare.

In April 2013, Ceregene announced the results of the trial: Neurturin had failed. Patients who had been treated with the drug did not improve any more significantly than those in a control group who had received a placebo treatment—a sham surgery in which a doctor drilled “divots” into the patient's skull so that it would feel as if there had been an operation. Ceregene was bought by another company in 2013, and its work on neurturin for Parkinson's has not been continued.

Poston was crushed. But then she looked at the data and noticed something that stopped her cold. Mike Pauletich hadn't gotten the real surgery. He had gotten the placebo.

**In a sense** both Pauletich and Mödl participated in a performance, one that we humans have been engaging in for thousands of years, every time we go to healers with the hope that they can make us feel better. And just as a good performance in a theater can draw us in until we feel we're watching something real, the theater of healing is designed to draw us in by creating powerful expectations in our brains. These expectations drive the so-called placebo effect, which can affect what happens in our bodies as well. Scientists have known about the placebo effect for decades and have used it as a control in drug trials. Now they are seeing placebos as a window into the neurochemical mechanisms that connect the mind with the body, belief with experience.

How does a belief become so potent it can heal? Back to the theater: A crucial part of an inspiring performance is sets and costumes. When Pauletich experienced improvement in his symptoms, it wasn't just because of the divots he could feel in his head or what the doctors told him about surgery. It was the whole scene he'd experienced: the doctors in their white coats, stethoscopes around their necks; the nurses, checkups, tests, maybe even the bad music in the hospital waiting room. Physicians sometimes call these trappings around hospitals the theater of medicine.

This stagecraft extends to many aspects of treatment and can operate on a subconscious level. Expensive placebos work better than cheap ones. Placebos in brand-name containers

work better than those labeled generics. Placebo suppositories work better in France, while the English prefer to swallow their placebos. Often fake injections work better than fake pills. But fake surgeries seem to be the most powerful of all.

Most astonishingly, placebos can work even when the person taking them knows they are placebos. This was reported in a now classic 2010 paper published by Ted Kaptchuk, a researcher at Harvard Medical School, and his team. After 21 days of taking a placebo, people with irritable bowel syndrome felt markedly better when compared with people who received nothing, even though those who reported feeling relief were told beforehand (and reminded afterward) that they were receiving placebos.

The experiment showed that a supportive patient-practitioner relationship was key in creating belief in a successful outcome. Patients were educated about the power of placebos and positive attitude. They were told that the placebo pills had been shown, in rigorous clinical testing, to induce meaningful self-healing processes. They were instructed to take the pills faithfully, missing no doses.

“Dealing with expectation is very tricky,” says Kaptchuk, who has spent his life studying placebo effects. “We’re dealing with very imprecise measuring of a very imprecise phenomenon. And a lot of it’s nonconscious.”

Karin Jensen, one of Kaptchuk's former colleagues who now runs her own lab at the Karolinska Institute in Stockholm, Sweden, designed an experiment to determine whether it was possible to use subliminal cues to condition subjects to experience a placebo effect.

During the conditioning phase of the experiment, subjects viewed alternating faces on a screen. Jensen used faces in her experiment because our brains are particularly adept at quickly recognizing them. Half the subjects received subliminal cues: The faces appeared for just a fraction of a second—not long enough to consciously tell them apart. For the other subjects, the facial cues appeared long enough for them to be consciously recognized.

During this first phase, varying heat stimuli were delivered to the subjects' arms along with the facial cues: more heat with the first face, less heat with the second. In the testing phase that followed, the subjects, including those who saw only the quick-flash subliminal cues, reported feeling more pain when they saw the first face, although the heat stimuli remained moderate and identical for both faces. The subjects had thus developed an unconscious link between greater pain and the first face.

The experiment showed that a placebo response can be conditioned subliminally. Jensen points out that tiny cues as you walk into a hospital—many of which are experienced unconsciously—trigger responses in our bodies in a similar way. “Part

of healing is nonconscious—something that happens instinctually,” she says.

**Hospitals are just** one common venue for the theater of belief. There are hundreds of alternative medical treatments that harness our expectations—homeopathy, acupuncture, traditional Chinese medicines, urine therapy, cow dung tablets, human blood facials, vitamin infusions, sound healing, to name a few—all with varying levels of proven efficacy.

“Belief is natural. It comes partly from the way our minds are hardwired,” says Tanya Luhrmann, an anthropologist at Stanford University who has dedicated much of her professional life to understanding people’s interactions with God.

She says that belief-based healing requires not only a good story but also the effort of an active listener—one with the ability to make what is imagined feel real. When story and imagination sync, the results can be astounding. “Humans have the capacity to change their experience,” she says. “These are skills, and we can learn them.”

I’d heard of the belief-based healing of the *brujos*, or witch doctors, of Catemaco, in the state of Veracruz on the eastern coast of Mexico. They are particularly theatrical healers, blending shamanistic traditions with Roman Catholicism much as Christians did a thousand years ago. I’d heard stories of massive, pentagram-shaped bonfires and dancing madmen who spit all over you as a blessing. Certainly worth a visit. But when

I arrived in Catemaco and made my way to a modern brujo's office, I found no fires or whooping shamans. Far from the dark, bat-infested cave I'd expected, the waiting area turned out to be a tidy little living room that smelled of disinfectant. Plastic amulets and glass crystals lined the shelves. About 10 people sat in chairs, reading magazines or watching soccer on TV. As witch doctors go, the brujo who greeted me looked more doctor than witch. Dressed all in white, he sported a neat mustache and short, heavily gelled hair. Half his office was taken up by an altar packed with crucifixes, statues of saints, flowers, and hundreds of blinking, colored lights.

I'd come for a simple *limpia*—a cleansing of my spirit. The brujo grabbed an egg, a few sprigs of basil, and a couple of plastic squirt bottles filled with what he said were envy blockers, bad-energy protection, and a liquid that makes wealth. Everything was orderly and sanitized. After a short interview, he got down to the business of my spirit, squirting me liberally with pungent oils and rubbing an egg over my body before cracking it open into a glass of water and examining the contents. I was familiar with this routine—it's common among brujos in Mexico. What surprised me was the lack of pomp or mumbo jumbo. It was more clinical than ceremonial. The brujo asked about my knees and lower back (both fine) and informed me that the egg indicated I might be in for some pain in the future. Like a radiologist explaining features on an x-ray, he noted several bubbles around the egg white in the glass: a sign that someone close to me was jealous and wished me ill. Then he offered, for an extra



fee, to protect me from future harm. I declined; we shook hands. I left feeling a sense of anticlimax, as if I had somehow missed something. Where was the theater? It was only when I was back on the street that I began to understand.

Twenty years ago you could still find “authentic” dancing, spitting witch doctors in Catemaco (and they still show up for tourists and festivals). But expectation is a moving target. Over the past generation, conventional medicine has become the norm in Catemaco. Spitting and waving chicken feathers inspired confidence before, but most brujos today have adapted to the times, mixing white lab coats and antiseptic spray with their mysticism to tap into their modern patients’ expectations: the theater of medicine. My brujo made eye contact and smiled warmly, like a skillful, caring medical doctor.

And I have to say, I did feel a little better.

**So how does the theater** of medicine actually work? How does a belief literally heal?

One part of the puzzle involves conditioning, as Jensen has shown. Recall Pavlov’s dog, which drooled every time it heard a bell. That happened because Pavlov conditioned the animal to connect food with the sound. Scientists have been able to train the immune systems of rats by pairing sweet liquids with cyclosporine A, a drug that blocks the function of immune cells to keep patients from rejecting transplanted organs. Every time the rat has a sweet drink, it also gets the drug. But after

enough trials, the drug is unnecessary: The sweet drink alone is enough to shut down the rat's immune response.

The placebo effect's conditioned response in reaction to pain is to release brain chemicals—endorphins, or opium-like painkillers—synthesized in the body. In the 1970s two San Francisco neuroscientists interested in how those internal opioids control pain made a discovery during an experiment with patients who had just had their wisdom teeth pulled.

The researchers first compared the response of a placebo group to the response of another group that received naloxone, a drug that cancels out the ameliorating effect of opioids. None of the subjects received or expected to receive morphine—and all of them felt miserable. Then the scientists redesigned the experiment, telling the patients that some of them would receive morphine, some a placebo, and some naloxone. No one, including the researchers, knew who would receive what. This time, some of the patients felt better, even though they didn't receive morphine. Their expectation of potential relief triggered the release of endorphins in their bodies, and those endorphins reduced the pain. But as soon as they got naloxone, they were in pain again. The drug wiped out the action of the endorphins that the placebo response had released.

“Without the expectation of pain relief, you can't have a placebo effect,” says Howard Fields, an emeritus professor at the University of California, San Francisco and one of the authors of the study.

Since that experiment, conditioning has been used to study the effects of belief on the release of other drugs produced by the body, including serotonin, dopamine, and some cannabinoids, which can work in a way similar to the psychoactive ingredient in marijuana. But it wasn't until the early 2000s that scientists could watch how these effects play out in the brain. Tor Wager, then a Ph.D. student at the University of Michigan, put subjects in a brain scanner. He applied cream to both of each subject's wrists, then strapped on electrodes that could deliver painful shocks or heat. He told the subjects that one of the creams could ameliorate pain, but the creams, in fact, were the same, and neither had any inherent pain-reducing qualities. After several rounds of conditioning, the subjects learned to feel less pain on the wrist coated with the "pain relieving" cream; on the last run, strong shocks felt no worse than a light pinch. A typical conditioned placebo response.

The most interesting part was what the brain scans showed. Normal pain sensations begin at an injury and travel in a split second up through the spine to a network of brain areas that recognize the sensation as pain. A placebo response travels in the opposite direction, beginning in the brain. An expectation of healing in the prefrontal cortex sends signals to parts of the brain stem, which creates opioids and releases them down to the spinal cord. We don't imagine we're not in pain. We self-medicate, literally, by expecting the relief we've been conditioned to receive.

“The right belief and the right experience work together,” says Wager, now a professor at the University of Colorado Boulder and director of a neuroscience lab there. “And that’s the recipe.”

The recipe of belief and experience is finding its way out of the lab and into clinical practice as well. Christopher Spevak is a pain and addiction doctor at the Walter Reed National Military Medical Center in Bethesda, Maryland. Every day he sees active service members and veterans with severe injuries, sometimes just days or weeks after they have left the battlefield. This offers him an opportunity to use expectation and conditioning to tap into internal opioids to stave off, or at least mitigate, long-term pain.

When Spevak first meets patients, he doesn’t ask about their injuries or their medical histories—he has all that on file. Instead he asks them about themselves. He might learn that in childhood a person had a favorite eucalyptus tree outside his house or loved peppermint candies. Eventually, if Spevak prescribes opioid painkillers, every time the patient takes one, he also has eucalyptus oil to smell or a peppermint to eat—whatever stimulus Spevak knows will resonate. Over time, just as with Jensen’s quick-flash faces or Wager’s skin cream (or for that matter, Pavlov’s bell), patients start linking the sensory experience to the drugs. After a while, Spevak cuts down on the drug and just provides the sounds or smells. The patient’s brain can go to an internal pharmacy for the needed drugs.

“We have triple amputees, quadruple amputees, who are on no opioids,” Spevak says of his Iraq and Afghanistan veteran patients. “Yet we have older Vietnam vets who’ve been on high doses of morphine for low back pain for the past 30 years.”

**Two years ago** Leonie Koban, a member of Tor Wager’s lab, spearheaded a novel placebo study. The scientists were well aware of the roles of conditioning and theater in channeling expectations. They wanted to test the effect of a third element influencing experiences of pain: other believers.

As in many previous tests of the placebo effect, the researchers delivered a burning sensation to their subjects’ arms and asked the subjects to rate how strong it was. But this time they introduced an extra variable. The volunteers looked at a screen and saw a series of hash marks representing how previous participants had rated their pain. For the same stimulus, the subjects reported feeling higher or lower levels of pain based on what they were told previous participants had felt.

The result was not surprising. In the 1950s, a series of tests called the Asch experiments showed that subjects can give answers they know to be wrong in order to conform with the group. What shocked Koban and Wager was the sheer strength of the social influence: The effect was larger than might be expected after conditioning. Tests of the subjects’ skin conductance responses—involuntary changes in how the body is conducting electricity, often used in lie detection—showed that they were not just reporting what they thought the researchers

wanted to hear; they were actually responding less to pain. Studies with fMRI machines implicated a separate, complementary network of brain activity that kicks in when conventional placebos are enhanced by peer pressure. Koban goes so far as to say that social information might be more powerful in altering the experience of pain than both conditioning and subconscious cues.

“Information we take from our social relationships has really profound influences, [not only] on emotional experiences but also on health-related outcomes such as pain and healing,” Koban says. “And we are only beginning to understand these influences and how we can harness them.”

