ANNALS OF SCIENCE

THE POWER OF NOTHING

Could studying the placebo effect change the way we think about medicine?

BY MICHAEL SPECTER

Scientists are now seriously investigating—and debating—our response to sugar pills.

ANDERS WENNGREN

For years, Ted Kaptchuk performed acupuncture at a tiny clinic in Cambridge, a few miles from his current office, at the Harvard Medical School. He opened for business in 1976, on a street so packed with alternative healers that it was commonly referred to as "quack row." Kaptchuk had just returned from Asia, where, as an exiled alumnus of the turbulent sixties, he had spent four years honing his craft. "There were lots of alternatives on that street in those days, but no practitioners of Chinese medicine," Kaptchuk, who is sixty-four and still lives in the neighborhood, told me recently as we sipped (Chinese) tea in the study of his house. "The area is a little too L. L. Bean for my taste now," he said. "It was a different place then."

Not long after Kaptchuk arrived in Boston, he treated an Armenian woman for chronic bronchitis. A few weeks later, she showed up in his office with her husband, who had a Persian rug slung over his shoulder. He nodded to Kaptchuk and said, "This is for you." Kaptchuk accepted the rug, which he still owns, but had no idea what he had done to earn it. "Oh, doctor, you have been so wonderful," the woman told him. "You cured me. I was about to have an operation on my ovaries and the pain went away the day you saw me." Kaptchuk never spoke to the woman again, but he has been unable to get her out of his mind. "There was no fucking way needles or herbs did anything for that woman's ovaries," he told me, still looking mystified, thirty-five years later. "It had to be some kind of placebo, but I had never given the idea of a placebo effect much attention. I had great respect for shamans—and I still do. I have always believed there is an important component of medicine that involves suggestion, ritual, and belief—all ideas that make scientists scream. Still, I asked myself, Could I have cured her? How? I mean, what could possibly have been the mechanism?"

At the time, few serious scientists would have entertained such questions, let alone allowed words like "ritual" and "belief" to seep into a conversation about medicine. Placebos had a bad name, which is not surprising, since they have been used primarily to deceive people. In clinical trials, if a drug and a sugar pill produce similar results, the drug has generally been considered worthless. But the definition of medical treatment is changing, and so are attitudes about placebos. This year, Harvard created an institute dedicated wholly to their study, the Program in Placebo Studies and the Therapeutic Encounter. It is based at the Beth Israel Deaconess Medical Center and Kaptchuk was named its director. He has already recruited leading researchers from around the world, in disciplines as diverse as neuroanatomy and semiotics. The program was formed to explore an idea that even twenty years ago would have seemed preposterous: that placebos—given deliberately—might be deployed in clinical practice. As medicine.

Kaptchuk has no shortage of critics. They acknowledge the power of the mind to influence health but question the rigor of studies suggesting that placebos could possibly prove as valuable as drugs. Indeed, the idea of dispensing sugar pills is jarring even to those who, like Kaptchuk, are enthusiastic about it. After all, placebos have almost always been defined as exactly what medicine is not. "I realized long ago that at least some people respond even to the suggestion of treatment," Kaptchuk said. "We know that. We have for centuries. But unless we figured out how that process worked, and unless we did it with data that other researchers would consider valid, nobody would pay attention to a word we said."

The research has been propelled in large measure by the emerging discipline

of neuroimaging—which, like a live satellite feed from inside the human body, permits scientists to track precisely how a person reacts to a drug (or a placebo) as soon as he takes it. An injection of saline, for example, that has been described as a drug not only will reduce symptoms of Parkinson's disease but can help a patient produce more of the dopamine that the disease destroys. Results like those have provided scientists with chemical evidence of something they had long suspected: simply believing in a treatment can be as effective as the treatment itself. In several recent studies, placebos have performed as well as drugs that Americans spend millions of dollars on each year.

Transforming interesting laboratory findings into medicine is never simple, however, particularly when those findings involve fake pills and sham injections. Some people clearly respond better to placebos than others, though we don't know why; some illnesses and afflictions are more amenable to suggestion than others; and many of the most intriguing findings are tenuous. Even so, the recent research is difficult to dismiss. Through conditioning techniques, for example, our brain can "learn" different kinds of placebo effects: people first given morphine and then a placebo have one neurochemical response, while people who take ibuprofen followed by a placebo have another. Different "doses" cause different reactions, and studies have demonstrated that people who suffer from headaches and consume aspirin regularly can associate the shape, the color, and even the taste of a pill with a decrease in pain. The value of treatments like those—which have none of the side effects of drugs—would be immense, but placebos are not pharmaceuticals, and no reputable researcher has suggested that they will soon be for sale at your local pharmacy.

Kaptchuk acknowledges that placebos are not magic potions. "Placebos don't shrink tumors," he said. "They don't make blind people see. If you are paralyzed, they won't help you walk." He deplores the grandiose claims of alternative medicine and prefers to rely on data. "Ultimately, I am not a zealot or even a true believer," he said. "I am sure that I do not understand the placebo effect. I ask questions, hopefully valuable questions, and we will see where the research lands."

Kaptchuk practiced acupuncture for half his adult life. But he stopped twenty years ago. Despite the popularity of acupuncture, clinical studies continually fail to demonstrate its effectiveness—a fact that Kaptchuk doesn't dispute. I asked him how a person who talks about the primacy of data and disdains what he calls the "squishiness" of alternative medicine could rely so heavily on a therapy with no proven value. Kaptchuk smiled broadly. "Because I am a damn good healer," he said. "That is the difficult truth. If you needed help and you came to me, you would get better. Thousands of people have. Because, in the end, it isn't really about the needles. It's about the man."

For most of human history, placebos were a fundamental tool in any physician's armamentarium—sometimes the only tool. When there was nothing else to offer, placebos were a salve. The word itself comes from the Latin for "I will please." In medieval times, hired mourners participating in Vespers for the Dead often chanted the ninth line of Psalm 116: "I shall please the dead in the land of the living." Because the mourners were hired, their emotions were considered insincere. People called them "placebos." The word has always carried mixed connotations. Thomas Jefferson wrote approvingly of what he called a "pious fraud," and noted that "one of the most successful physicians I have ever known has assured me that he used more bread pills, drops of coloured water, and powders of hickory ashes, than of all other medicines put together." But, as increasingly specific knowledge about human anatomy emerged, people began to demand scientific answers to medical questions. Knowledge displaced faith, and human health improved rapidly. Antibiotics are real; placebos are not.

The first publicly acknowledged placebo-controlled trial—and still among the most remarkable—took place at the request of King Louis XVI, in 1784, under the direction of Benjamin Franklin, then the American Ambassador to France. The German physician Franz Anton Mesmer had become famous in Vienna for a new treatment he called "animal magnetism," and he claimed to have discovered a healing fluid that

could "cure" many ailments. Mesmer became highly sought after in Paris, where he would routinely "mesmerize" his followers—one of whom was Marie Antoinette. The King wasn't buying it, however, and he asked a commission of the French Academy of Sciences to look into the claims. (The members included Franklin, the chemist Antoine Lavoisier, and Joseph Guillotin—who invented the device that would eventually separate the King's head from his body.) The commission replicated some of Mesmer's sessions, and, in one case, asked a young boy to hug magnetized trees that were presumed to contain the healing powers invoked by Mesmer. He did as directed and responded as expected: he shook, convulsed, and swooned. The trees, though, were not magnetic, and Mesmer was denounced as a fraud. Placebos and lies were intertwined in the public mind.

It was another hundred and fifty years before scientists began to focus on the role that emotions can play in healing. During the Second World War, Lieutenant Colonel Henry Beecher—who went on to become the first chairman of the anesthesia department at Massachusetts General Hospital—attempted to assess the degree to which the severity of a soldier's injuries corresponded to the amount of pain he felt. In Europe, Beecher met with more than two hundred soldiers, gravely wounded but still coherent enough to talk; he asked each man if he wanted morphine. Seventy-five per cent declined.

Beecher was astounded. He knew from his experience before the war that civilians with similar injuries would have begged for morphine, and he had seen healthy soldiers complain loudly about the pain associated with minor inconveniences, like receiving vaccinations. He concluded that the difference had to do with expectations; a soldier who survived a terrible attack often had a positive outlook simply because he was still alive. Beecher made a simple but powerful observation: our expectations can have a profound impact on how we heal.

Armed with this information, and with his conviction that the placebo effect could be harnessed to help relieve suffering, Beecher returned to the United States and continued his research. In 1955, he published an article called "The Powerful Placebo," in which he wrote that "placebos have a high degree of therapeutic effectiveness in treating subjective responses." The paper has been cited more than a thousand times by other scientists, and Beecher's conclusion—that the placebo effect plays a critical role in almost any medical intervention—influenced much of what has followed in clinical research. His basic supposition was correct: emotions and expectations can affect our perception of pain.

Before Beecher's work, new drugs were tested in a haphazard manner; since then, they have always been compared with a placebo or with another drug. But Beecher's methodology was deeply flawed. Although he reported that placebos were effective more than a third of the time, he shrugged off a phenomenon known as "regression to the mean." Over time, the condition of most patients improves, with or without treatment. A person who enrolls in a clinical study when he is feeling particularly bad is likely to improve solely as a result of the natural course of the illness, not because he was given a placebo. (And people often enroll in such studies when they are sickest.) A patient who knows that he is in a study also may expect a better therapeutic result than one who doesn't. If you believe that doctors are particularly attentive, you can get better more rapidly, even if they aren't. This is known as the Hawthorne effect. (There is also a "nocebo effect." Expecting a placebo to do harm or cause pain makes people sicker, not better. When subjects in one notable study were told that headaches are a side effect of lumbar puncture, the number of headaches they reported after the study was finished increased sharply.)

For years, researchers could do little but guess at the complex biology of the placebo response. A meaningful picture began to emerge only in the nineteen-seventies, with the discovery of endorphins: substances secreted in the brain that are chemically similar to opiates like morphine and heroin. The discovery led to the novel idea that, in effect, the brain produces its own pharmacy. In 1978, three scientists from the University of California at San Francisco—Jon Levine, Newton Gordon, and Howard Fields—decided to investigate whether endorphins might explain why patients who received placebos often reported a significant reduction in pain. People recovering from dental surgery were told that they were about to receive a dose of morphine, saline, or a drug that might increase their pain. By then, researchers had learned not only about the nocebo effect but that a suggestion of relief will often trigger the production of endorphins, so they were not surprised that patients receiving saline reported reduced pain.

What came next, however, fundamentally reshaped the field. The researchers dismissed the subjects who received morphine and then divided the remaining participants into those who responded to the placebo and those who didn't. Then they introduced Naloxone into patients' I.V. drips. Naloxone was developed to counteract overdoses of heroin and morphine. It works essentially by latching onto, and thus locking up, key opioid receptors in the central nervous system. The endorphins that we secrete attach themselves to the same receptors in the same way, so Naloxone blocks them, too. The researchers theorized that, if endorphins had caused the placebo effect, Naloxone would negate their impact, and it did. The Naloxone caused those who responded positively to the placebos to experience a sharp increase in pain; the drug had no effect on the people who did not respond to the placebo. The study was the first to provide solid evidence that the chemistry behind the placebo effect could be understood—and altered.

"It was one of those studies that make the scales fall from your eyes," Kaptchuk told me. "I had just started to think about the placebo effect—scientifically and historically. And here comes this paper that says that, even if it's all in your head, there is still a biological mechanism driving these reactions. It was very exciting."

Kaptchuk assumed that the results would add legitimacy to the field. He was wrong. "Things are better than they were," he said. "But even now, you know, people at Harvard talk about placebos the way the Popes used to talk about medicine. They declared that Jews were not allowed to treat Christians—not because they were not good doctors but because it would have been ethically wrong. These are ethical judgments masquerading as science. Because from the

beginning I kept having this nagging thought: what is so bad about getting better from a placebo?"

That kind of thinking, still hard for most doctors to accept, was heretical in 1990, when Kaptchuk arrived at Harvard. "People kept saying, 'Oh, this is just the placebo effect.' You would hear that every day," Kaptchuk said. He had spent years studying Chinese medicine (and medical history), and this made no sense to him. "I thought, Ted, step back a minute. This wasn't just something that was a negative. It was something that needed to be understood."

Slowly, over the past decade, researchers have begun to tease out the strands of the placebo response. The findings, while difficult to translate into medicine, have been compelling. In most cases, the larger the pill, the stronger the placebo effect. Two pills are better than one, and brand-name pills trump generics. Capsules are generally more effective than pills, and injections produce a more pronounced effect than either. There is even evidence to suggest that the color of medicine influences the way one responds to it: colored pills are more likely to relieve pain than white pills; blue pills help people sleep better than red pills; and green capsules are the best bet when it comes to anxiety medication.

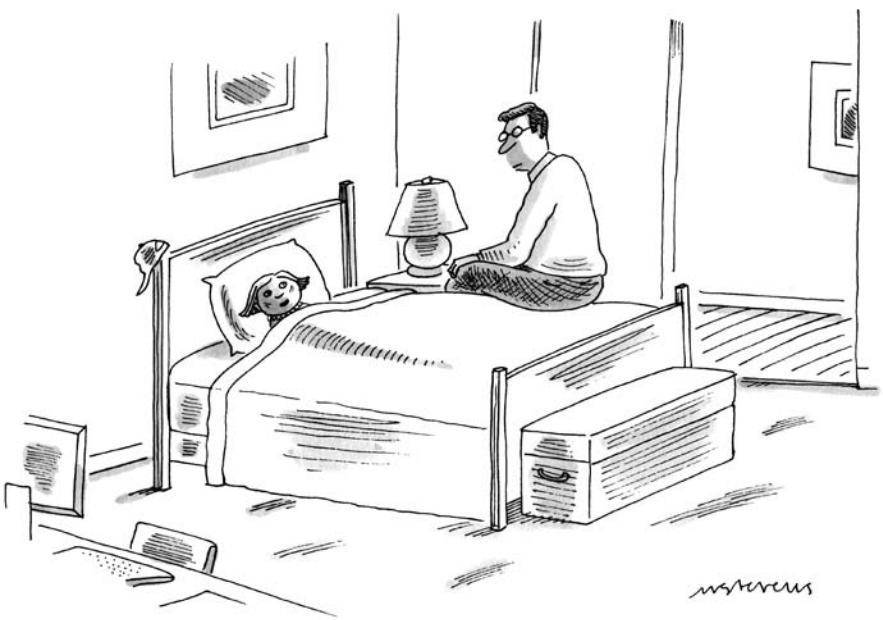
Conditioning and expectations matter, and so does learned behavior. In the eighties, Levine and Gordon divided a group of postoperative patients into three sections: those in the first section received morphine secretly, those in the second were told they would receive morphine (and did), and those in the third were given a placebo that was described as a powerful pain reliever. The results were startling. Patients who were told that they would receive a painkiller, whether they actually received it or not, had the same experience in the trial as those who secretly received between six and eight milligrams of morphine—a significant amount. The covert dose had to be increased to twelve milligrams to surpass the effect of the placebo. Over the past two decades, the Italian neuroscientist Fabrizio Benedetti (who studied with Gordon and Levine), and Luana Colloca, a colleague of Benedetti's, who is now based in the United States, at the National Institutes of Health, have expanded on these studies. They have found, for example, that diazepam—more commonly known as Valium—has no discernible effect on anxiety unless a person knows he is taking it. And, increasingly, studies like those have been carried out with the help of imaging techniques—such as PET scans and functional M.R.I.s—that can track brain changes as they happen. These advances in brain imaging, along with an increased understanding of neurochemicals, have transformed a vague and mysterious notion into a tangible effect that scientists consider worthy of investigation.

"What's exciting here is that, if we are to talk about using placebos in a clinical setting, they would have to have a measurable effect and a biology we understand," Wayne Jonas told me. Jonas is an interesting hybrid in a world often sharply divided between conventional and alternative therapies. In the early nineties, he served as the director of the Medical Research Fellowship Program at the Walter Reed Army Institute of Research, in Washington, D.C. He went on to run the Office of Alternative Medicine at the National Institutes of Health, from 1995 to 1999. Today, Jonas is the president of the Samueli Institute, a Washington research group devoted to shifting the focus of health care from treatment to prevention.

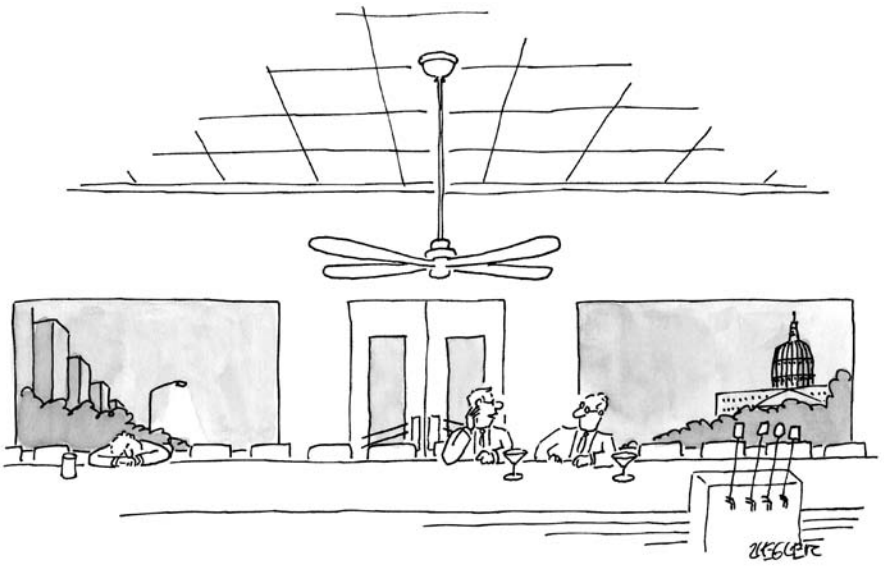
"The morphine studies bring us a long way," he said. So did a recent investigation by Kaptchuk, in which participants suffering from irritable-bowel syndrome were not deceived about their treatment; in fact, they were told in great detail about the placebos they received and that they were often as effective as real medicine. The pills brought them relief.

For many people in the field, results like those achieved in the morphine and I.B.S. studies, while preliminary and in need of confirmation, hint at something far more significant than the effect of a placebo or problems with a particular drug. They suggest that the "magic bullet" approach to health care—simple, effective solutions to single problems, like a strep infection or polio—can no longer remain our principal approach to treating disease.

There has always been a distinction between disease and illness. Disease is a biological condition that we have historically treated with drugs, surgery, and other technological solutions. Illness, on the other hand, defines the context of a medical encounter, including the relationship between doctor and patient. Like Kaptchuk, Jonas believes that placebo research demonstrates that it is essential to consider both the science and the art of medicine—to think about diseases as illnesses, and not to rely solely on short-term, high-tech solutions. Scientists hope that, even if it proves impossible to replace drugs with placebos, research into the way they affect us will accomplish nothing less than a transformation of American medicine. "There are



"Bore me to sleep, Daddy."



"He's the chief watchdog, who watches over all the other watchdogs—but this must be his night off."

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no magic bullets for most of the problems that ail us today," Jonas said. "Diabetes, immune-system disorders, chronic pain, cancer. Our illnesses are complex, and we need to approach them in more comprehensive ways. We try to identify drugs that will eliminate disease. Yet the way we go about delivering those agents—the interaction between doctor and patient, for example—often has a bigger impact than the agent we focus on. More than the drug and more than the surgery. And that has been collectively called the placebo effect."

The headquarters of the Food and Drug Administration, situated on a campus called White Oak, on the far edge of Silver Spring, Maryland, seems as close to the rest of the federal medical establishment as it is to Pluto. There is no Metro to White Oak, and it takes half an hour to drive from the sprawling campus to the National Institutes of Health, in Bethesda. The F.D.A.'s physical isolation belies its position as the nation's principal regulator of consumer products. No drug is sold without the agency's approval. There will be no prescriptions for any placebo, either, unless clinical trials have demonstrated its effectiveness to the satisfaction of the F.D.A.

"One of the absolutely fundamental problems that we have is the use of the term 'placebo,' which does nobody any good," Robert Temple told me, echoing a complaint made by virtually everyone who deals with the subject. Temple, who has for many years run the F.D.A.'s drug-evaluation department, is an owlish man with a short, thick mustache and circular glasses. His office is so filled with towering stacks of files that, after you enter, it takes a moment to find him. "Just because something is called a 'placebo group,' " he said, "everyone assumes that what happens in that group is a result of the placebo effect. And that is absolutely not true."

Temple, who has worked at the F.D.A. for four decades, rarely makes a decision without angering somebody. He has been regarded as a meddlesome reactionary by H.I.V. activists and others who insist that drugs be released more rapidly. The more conservative medical establishment frequently accuses the agency of endorsing the wishful thinking of drug manufacturers. And to the large and growing community that supports alternative approaches to medicine Temple is Dr. No.

Temple said that he understands why placebos attract people who become frustrated when science fails to provide definitive answers. "The persistence of what people believe will save their lives as opposed to the evidence is staggering," he said. "So people are talking about using placebos as drugs. But I have no idea what that means in practical terms. How would it work?" Tantalizing hints and possible effects are not data, and Temple says there are no data that would suggest that placebos are drugs. There are several studies, though, that illustrate the basis for his skepticism.

A placebo effect is commonly observed during trials of blood-pressure medications. To qualify for such studies, subjects are supposed to have blood pressure that exceeds a hundred and forty over ninety in at least one of the two measurements. "As soon as somebody enters those studies, his or her blood pressure falls an average of five or six millimetres of mercury," Temple said. "That is significant, but it is not a placebo response, and it is not a response to being in the study. It is often the result of doctors' inflating readings—of rounding up." If a person's blood pressure is a hundred and thirty-eight over eighty-eight, for example, investigators will often include him. "When you use an automatic blood-pressure cuff to establish a baseline for these kinds of studies, the entire placebo effect vanishes," Temple said.

When a drug (or a placebo) is under study, subjects are usually divided into two groups. Neither group knows exactly what it is getting (nor do the doctors), but one group generally receives the drug and the other a placebo. "There is a better way," Temple said. "If you want to see if there is a placebo effect, use three arms in a drug trial, not two. Tell them, 'Some of you will be getting a drug, some will get a tablet that looks like a drug but is nothing but a sugar pill, and some of you will get nothing at all.'

"It seems to me," he went on, "that if there is any substantial placebo effect, there ought to be a difference between the group that knows it's getting nothing and the group that doesn't know it's getting nothing. If there is no difference, then what are we talking about? Because it's not a placebo effect."

It turns out that there have been many trials of the type Temple mentioned. In 2001, the Danish epidemiologist Asbjørn Hróbjartsson, of Copenhagen's Nordic Cochrane Center, along with his colleague Peter Gøtzsche, published a systematic review of a hundred and fourteen clinical trials that compared patients who received a placebo with subjects who

were told that they would receive no medicine at all. The researchers attempted to assess the combined impact of many different kinds of trials using meta-analysis, a statistical technique for extracting information from studies that are not statistically significant by themselves. Their article, "Is the Placebo Powerless? An Analysis of Clinical Trials Comparing Placebo with No Treatment," published in *The New England Journal of Medicine*, was a long-overdue response to Beecher's 1955 paper.

In almost every case, the researchers reported, there was essentially no difference between the placebo group and the openly untreated group. There were particular exceptions in studies of pain, where there was a slight but measurable placebo effect. Since we are physiologically capable of manufacturing our own painkillers—endorphins—the result may not have been surprising. Expectations and suggestion clearly influence behavior, and when we expect to receive medicine our bodies often begin to prepare for it. (As the evolutionary biologist Robert Trivers recently pointed out, in "The Folly of Fools," his book about the historical necessity of deceit, what the brain expects to happen in the near future affects its physiological state. Trivers's theory would explain a fact that has often baffled scientists: the placebo effect doesn't appear to work with Alzheimer's patients. Trivers suggests that this is because most people who have Alzheimer's disease are unable to anticipate the future and are therefore unable to prepare for it.)

The Danish researchers repeated the study in 2004, and again last year, incorporating new data each time. The results and their conclusions remained the same. "We found little evidence in general that placebos had powerful clinical effects," Hróbjartsson wrote. "Outside the setting of clinical trials, there is no justification for the use of placebos."

Kaptchuk has great respect for Hróbjartsson, yet he is wary of relying on meta-analyses, and he believes that an honest interaction between a doctor and a patient can significantly alter the outcome of treatment. That was the point of his study of irritable-bowel syndrome, in which some subjects were told that they would not be treated. I.B.S., a chronic gastrointestinal disorder, is one of the most common reasons that people seek medical care. Effective long-term therapies have proved elusive. In Kaptchuk's study, eighty patients were randomly divided into two groups. Patients in the first group received a placebo pill twice a day; those in the second received nothing. Before the study began, both groups were told that placebos were "inert or inactive pills, like sugar pills, without any medication in them." They were also informed that placebos have been shown in "rigorous clinical testing to produce significant mind-body self-healing processes." Patients who received the openly distributed placebo scored far better on standard assessments of their condition than those who received nothing. There were also statistically significant differences in the severity of symptoms.

Although a group of eighty patients is too small to draw definitive conclusions, honesty seemed to work. "Asbjørn's stuff is a constant intellectual challenge," Kaptchuk wrote in an e-mail. "His meta-analyses are tops. Great methods, very careful. Clear." Yet Kaptchuk also pointed out that placebos are not the only interventions that can cause complicated reactions. Drugs do, too. Opiods, for example, increase pain in about ten per cent of those who take them. Antibiotics don't always work, and neither does cortisone, a powerful steroid used each year by millions of people. Meta-analyses are useful to help understand large amounts of data from different trials. But statistical results that combine information from a variety of medical centers, with different kinds of patients, often in different countries, administered under different conditions, cannot be uniform and therefore cannot be conclusive.

Hróbjartsson and Kaptchuk are united on at least one front. Like Wayne Jonas, they agree that the medical system needs to change. "You have to put this into the context of the society in which you live," Hróbjartsson told me. "Because I think this may be as much a matter of philosophy as of science. There is an anti-technological, anti-science feeling in the West. We constantly see frustration with the limits of medicine. The placebo can be seen in some sense as a logical avenue for those frustrations. Everyone wants a simple, pain-free solution. But I wonder if that approach isn't just the mirror image of the pharmacological way of handling illness—that there is a pill for every disease.

"The entire idea of a placebo is very 'soapy,' " Hróbjartsson continued. "It slips away whenever you try to find a border."

That has always been true. After all, for many people a placebo is just a sugar pill. For others, the definition includes the entire ritual of treatment, the complete interaction between doctor and patient. Increased attention has mostly raised new questions: What are the physical and psychological mechanisms that produce placebo effects? What are the conditions they most easily affect? And can we actually identify people who respond to placebos? Scientists now have bits of answers to some of those questions, but to reach their goal, and introduce placebos into clinical practice, they will need to answer all of them.

Ted Kaptchuk gets a great deal of pleasure from focussing on what other people reject. Indifference seems to motivate him. "I was raised in a crazy home, and it prepared me to accept any proposition," he said. That, he once told me, is why he was so active in the sixties: "It was a time when the underpinnings of the universe were questioned." Both of Kaptchuk's parents, who were Poles, survived the Holocaust. "That really defines a lot of what I do. My father was a Red, so I have a tendency to get pleasure from subversiveness."

A particularly radical son of the sixties, Kaptchuk was one of the founders of the Columbia University chapter of Students for a Democratic Society, in 1965, but the organization was soon dominated by a faction that became the Weather Underground. That was too radical even for Kaptchuk. He fled to the West Coast. "I was hanging out with the San Francisco Red Guards and reading Mao, trying to get away from U.S. imperialism," he said. "I was militant and crazy. But at some point I said, Ted, this is not being human."

Kaptchuk decided to pursue studies in Chinese philosophy and medicine at the source. Beijing had yet to open its borders to Americans, but Kaptchuk hoped that his revolutionary bona fides would prompt the leadership to make an exception. "My request to study there was de-

livered to the government by members of the Black Panther Party," he told me. Even that didn't work. The Chinese denied the request, and Kaptchuk spent much of the next decade studying in Macau.

Today, it is hard to imagine Ted Kaptchuk as a radical, let alone a fugitive. He is an observant Jew who wears a yarmulke on top of a shaggy bowl haircut that looks as if he'd copied the Beatles, circa 1964, then let it grow. As a devotee of Eastern thought, he bars shoes from his house and speaks in a hushed, measured voice. David Carradine would have played him beautifully.

Kaptchuk is the first prominent professor at Harvard Medical School since Erik Erikson with neither a medical degree nor a doctorate, and it would be easy to dismiss him as a signature representative of the unsubstantiated-alternative-health-care movement. But he has published scores of books, articles in highly regarded peer-reviewed journals, letters, and review notes—on subjects ranging from placebo research to exorcism, from cancer treatment to shaman rituals among Navajo Indians. He has just finished a study designed to answer a central question in placebo research: Do the genes of people who respond to placebos differ in significant ways from those of people who don't? (The data, compelling but so far preliminary, suggest that the answer is yes.)

"Ted Kaptchuk is the most knowledgeable person in the world on all matters placebo," Franklin Miller told me. Miller is a senior faculty member in the Department of Bioethics at the National Institutes of Health. "He has done the research, the scholarship, and the most interesting and clinically relevant studies." One day, I asked Kaptchuk how a man who practiced acupuncture and dispensed herbs, rather than earning a Ph.D. in biology or statistics, had learned to design complicated trials. He told me that he spent years seeking the advice of the most highly respected and rigorous medical statisticians. "I basically apprenticed myself," he said, "and they were happy to help a quack who wanted to deal with data."

Kaptchuk is proud of being what he calls "a card-carrying member of the Harvard establishment." It is a distinction that did not come easily, even though he has received millions of dollars in funding for his projects from the National Institutes of Health. "The goal is to understand placebos so that they may be used intelligently," he said one day. "But this is the area where I veer from some of my colleagues. Because what do I really want? Anything that gets people away from the conveyor belts that move from the pharmaceutical houses to doctors and on to patients is worth considering. Anything. We need to stop pretending it's all about molecular biology. Serious illnesses are affected by aesthetics, by art, and by the moral questions that are negotiated between practitioners and patients. Chiropractors never say that your pain is all in your head. But orthopedists do it all the time. What a fucking way to try and help somebody heal. Do you know how evil that is?"

That kind of deeply held conviction touches on the fundamental questions that challenge American medicine. Kaptchuk wants to broaden the definition of healing, which is exactly what enrages many scientists. In one recent study of a major asthma drug, he and his colleagues reported that, although placebos had no impact on the chemical markers that indicate whether a patient is responding to therapy, patients nonetheless reported feeling better. Kaptchuk concluded that objective data should not be the only criterion for doctors to consider. "Even though objective physiological measures are important," he wrote in the study, published earlier this year in *The New England Journal of Medicine*, "other outcomes such as emergency room visits and quality-of-life metrics may be more clinically relevant to patients and physicians."

"My jaw dropped when I read this," David Gorski, a professor of medicine at Wayne State University School of Medicine, wrote on the science blog Respectful Insolence. " 'Other outcomes' besides objective measures of disease severity may be 'more clinically relevant'?" That kind of assertion clashes with the basic truths of the scientific method. Kaptchuk counters that we are losing sight of our goal—which is to make people feel better. "This study demonstrated that, without a change in objective data, you still get incredible subjective improvement," he said. "So is a doctor really supposed to say, Gee, the patient is feeling good but I better ignore that and go by the numbers?"

It was late in the afternoon, and we were sitting in Kaptchuk's garden in Cambridge. He looked at me and threw his hands into the air. "Is my approach just hocus-pocus?" he said softly. "Isn't that what you are really asking? You want to know the relationship between rationality and feeling and between science, critical thinking, and the art of medicine. And that boils down to one question: Do you think this entire field is based on a foundation of magical thinking, or do you not?"

Three years ago, a week before Thanksgiving, while I was sitting in my office, my chest began to throb. It was a diffuse pain, but pain nonetheless. I am a middle-aged man with the usual amount of stress (too much) and I handle it in the usual way (denial). My cholesterol and blood pressure are normal, and I exercise regularly and try to eat sensibly. Still, I have read many obituaries of "healthy" men my age who ignored chest pain. So, somewhat sheepishly, I called my doctor and explained the situation, and he told me to come right over.

He conducted a thorough examination, and then we talked. He told me I was fine, that Thanksgiving is often a tense time, and that I should relax. My pain suddenly disappeared. I have written frequently of my belief that magic is for fairy tales and science is for humans. But something about that process soothed me. Of course, it was a relief to know that I wasn't sick. But could words really banish a pain I had struggled with for hours?

After I got home, I realized that I had been given a placebo. Not purposefully, perhaps, but it had the same effect. My doctor told me that I was fine, and that made my pain go away. It also eased my anxiety at least as effectively as if I had swallowed a pill. My doctor takes an extremely science-based approach to his work. That's what makes him so good at his job. But that afternoon we engaged in exactly the type of ritual that, according to Kaptchuk, will have to play a critical role in the future of American health care. And, at least in this instance, it would have been hard to argue that it didn't work. ♦