

# Brain Powered

A wave of recent advances shows how the mind affects health in ways we never imagined.

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By Dan Ferber, PhD From [Reader's Digest](#)

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## Mice, Maps, and Major Milestones

**It's been a very good year for the brain -- that three-pound wrinkled lump of gray matter that directs our movements, thoughts and memories, our loves, hopes and dreams. It's the organ that makes us who we are. It can also make us lose who we are, through degenerative diseases like Alzheimer's, which affects almost half of those who live past 85. And now we know it has far more to do with our overall health than we ever imagined.**

A recent wave of breakthrough technologies has yielded unprecedented insight into how our brains work, and a better grasp of how they go wrong. That, in turn, has led to new targeted treatments designed to fix malfunctions. Science is also revealing the surprising power of the mind, when used correctly, to heal the body. Here are some of the mind-boggling findings.

### Mapping the Brain

September 2006 marked a major milestone for our noggins, with completion of the Allen Brain Atlas, the first gene map of the brain. It all started in 2002, when billionaire philanthropist Paul Allen, cofounder of Microsoft, gathered some of the world's top scientists and charged them with finding an innovative new way to accelerate our understanding of the brain. From that he committed \$100 million and established the Allen Institute for Brain Science in Seattle.

Using custom-built robotics and software, 60 full-time researchers tested 250,000 preserved slices of mouse brain, which resembles the human one enough that most discoveries would also hold true for us. They generated a volume of raw data that revealed where in the brain each of the mouse's 21,000 genes was activated. (Different types of brain cells activate different sets of genes, producing a unique roster of proteins that enables each cell to do its job -- storing memory, directing movement or some other task.)

The map revealed that about 80 percent of the body's genes are turned on in the brain -- more than anyone had expected. That means if pharma companies are not careful, drugs targeted to other organs could have unwanted side effects in the brain. The map also uncovered evidence that could help reveal what goes wrong in complicated brain disorders such as schizophrenia and autism.

The result is a 3-D virtual mouse brain atlas ([brain-map.org](http://brain-map.org)) that does for neuroscientists what a survey map pinpointing gold deposits does for miners: It lets them hightail it to where the action is and start digging, says David Anderson, PhD, a professor of biology at California Institute of Technology and a project advisor.

Targeted gene therapies could help patients with brain diseases that drugs alone cannot heal. Such therapies deliver healthy genes to parts of the body where faulty ones are wreaking havoc. In the past, gene therapies turned out to be more dangerous than scientists had expected, and the death of an Arizona teenager in a 1999 clinical trial set the field back years. But a new method of gene delivery to the brain, via a harmless virus called adeno-associated virus (AAV), has proved safe in early human trials.

One AAV therapy may ease advanced Parkinson's disease by repairing an overactive brain circuit that causes typical symptoms of slowness and rigidity. That circuit acts like a brick on a car brake, interfering with the patient's ability to move. Brain surgeons currently remove that brick by implanting a pacemaker-like device that overrides this circuit. But the treatment, called deep brain stimulation, requires three months of weekly visits to a

specialized neurosurgery facility, which is tough when you live hundreds of miles away, says neurosurgeon Michael Kaplitt, MD, of Weill Cornell Medical College.

Dr. Kaplitt's AAV therapy removes the brick from the brake by delivering a neurochemical called GABA into brain cells. In a safety trial that ended in 2006, the gene therapy proved safe. At the highest levels, it helped patients as much as deep brain stimulation. If this proves effective in a larger trial, someday an advanced Parkinson's patient could have brain surgery, get a gene implanted in precisely the right spot and go home a couple of days later. "Our hope is to bring this type of therapy to a much larger audience of patients in need," Dr. Kaplitt says.

Since his trial, other AAV gene therapies have been used in six early trials: three for Parkinson's, two for lethal pediatric brain disorders and one for Alzheimer's. If they continue to prove safe and show positive results, we'll be able to treat some of the most devastating brain disorders.

### **Bridging the Blood-Brain Barrier**

Scientists have begun to overcome one of the biggest obstacles to treating brain disease: getting drugs into the brain. Ninety-eight percent of candidate drug compounds do not pass from the bloodstream into the brain, even though they move easily into other organs, says William Pardridge, MD, a professor of medicine at University of California, Los Angeles. As a result, good drugs for brain disorders are few and far between. Would-be drugs fail because the walls of the brain's blood vessels act like border-crossing guards after a code-red terror alert: They allow only molecules that have essential business in the brain to cross. To get his drugs past the hypervigilant guards, Dr. Pardridge turned to smuggling. He uses genetic engineering to link potentially helpful brain drugs to a specific kind of antibody that is welcomed and escorted into the brain.

In a 2006 study, one such hybrid drug reduced brain damage by two-thirds in rats when given two hours after a simulated stroke. The drug contains a normal brain protein that stimulates cells to thrive but is normally too scarce to prevent stroke-induced brain damage. Such brain-cell-saving drugs are desperately needed to protect stroke patients from brain damage, but over the past decade, none have passed muster in clinical trials. ArmaGen Technologies, which Dr. Pardridge founded to commercialize the technology, plans a human safety trial on the new stroke drug in late 2007.

The smuggling strategy could work with any brain drug, Dr. Pardridge says, and ArmaGen is developing drugs for Alzheimer's, Parkinson's and a class of hereditary brain diseases that cause birth defects, mental retardation and other severe problems.

In one of brain biology's most amazing advances, scientists have found that our brain may actually help our immune system fight disease. It took 20 years of careful experiments for Kevin Tracey, MD, to see it that way. It also took a very special patient -- an 11-month-old girl named Janice. "She changed my life," says Dr. Tracey, a neurosurgeon, immunologist and director of the Feinstein Institute of Medical Research in Manhasset, New York.

In the spring of 1985, Dr. Tracey was a surgeon in training at New York Hospital, treating patients for such things as gunshot wounds, head injuries and infection, when Janice was admitted. She had been crawling on the kitchen floor of her grandmother's Brooklyn apartment when her grandmother, who was cooking pasta, tripped over her and spilled a ten-quart pot of boiling water onto the baby girl. Dr. Tracey cared for the girl, who had suffered second- and third-degree burns over 75 percent of her body. A week after she was admitted, Janice developed severe sepsis, a condition in which the immune system massively overreacts to a bacterial infection, indiscriminately training its cannons on the body's own tissues.

For the next two and half weeks, Janice lay clinging to life in her hospital bed, as Dr.

Tracey and his colleagues tried one heroic measure after another to revive her. She recovered enough to celebrate her first birthday in the burn unit with her parents, her grandmother and the medical staff, and was expected to be discharged soon. Then, the next day, her heart stopped suddenly and she died. "She's the only patient I ever had nightmares about," Dr. Tracey says. "She shouldn't have died."

No one knew then what caused severe sepsis, so, inspired by Janice, Dr. Tracey set out to learn. Two decades later, his work is paying off. In a series of studies since 2000, he's shown that stimulation of the vagus nerve -- a major nerve that runs from our brainstem to our belly and regulates our heartbeat, breathing and intestines--stops severe sepsis. It does so by using neurochemicals to signal immune cells, which prevents them from releasing alarm molecules that spur inflammation and cause damage. In a 2006 study, he discovered a brain circuit that could stimulate the vagus nerve to switch off inflammation.

Taken together, the studies demonstrated a hard-wired connection between the brain and immune system that Dr. Tracey calls the "inflammatory reflex." Normally, when inflammation spreads, the brain tells the immune system to turn it down. In patients like Janice with severe sepsis, that reflex fails.

Drugs that activate the reflex could one day reduce chronic low-grade inflammation--the kind that causes Crohn's disease and rheumatoid arthritis, and contributes to heart disease. Meditation might help, too, says Dr. Tracey. People can learn to slow their heartbeat by modifying vagus nerve activity, which suggests they might be able to control their own brains to calm inflammation and fight disease. "It's the most exciting thing I've ever worked on," he says.

Calming the mind and body might even slow the spread of some cancers. The stress hormone norepinephrine can spur lab-grown cancer cells to release two compounds that help them move through the body and then metastasize, according to a study in the November issue of *Cancer Research* by virologist Ronald Glaser, PhD, of Ohio State University Medical Center. A third compound that's released helps supply growing tumors with nutrients. So reducing stress may prove a cancer fighter.

Studies like Glaser's and Dr. Tracey's have "given credibility to mind-body approaches, which had been rejected and ignored by the scientific and medical communities," says Esther Sternberg, MD, director of the Integrative Neural Immune Program at the National Institute of Mental Health. Now scientists and doctors have begun taking the next step, harnessing the immense powers of the human brain to help people heal themselves. For example, using special fMRI scanners and software that allowed patients to see their own brain activity, scientists at Stanford University and Omneuron, a biotech company, trained participants to reduce chronic pain by just visualizing it and learning to control it. Some were able to decrease it by more than 40 percent, says pain expert Sean Mackey, MD, one of the study leaders.

Dr. Mackey foresees a day when doctors might use such imaging to train us to ease depression, battle addiction or overcome phobias. And years from now, he says, we may head to a real-time brain-imaging center the way we go to the fitness center today, and buff up parts of our brain that improve performance, memory and even intelligence. Now, that would be a real no-brainer.