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Can the Nervous System Be Hacked?

By: Michael Behar

One morning in May 1998, Kevin Tracey converted a room in his lab at the Feinstein Institute for Medical Research in Manhasset, N.Y., into a makeshift operating theater and then prepped his patient — a rat — for surgery. A neurosurgeon, and also Feinstein Institute's president, Tracey had spent more than a decade searching for a link between nerves and the immune system. His work led him to hypothesize that stimulating the vagus nerve with electricity would alleviate harmful inflammation. "The vagus nerve is behind the artery where you feel your pulse," he told me recently, pressing his right index finger to his neck.

The vagus nerve and its branches conduct nerve impulses — called action potentials — to every major organ. But communication between nerves and the immune system was considered impossible, according to the scientific consensus in 1998. Textbooks from the era taught, he said, "that the immune system was just cells floating around. Nerves don't float anywhere. Nerves are fixed in tissues." It would have been "inconceivable," he added, to propose that nerves were directly interacting with immune cells.

Nonetheless, Tracey was certain that an interface existed, and that his rat would prove it. After anesthetizing the animal, Tracey cut an incision in its neck, using a surgical microscope to find his way around his patient's anatomy. With a hand-held nerve stimulator, he delivered several one-second electrical pulses to the rat's exposed vagus nerve. He stitched the cut closed and gave the rat a bacterial toxin known to promote the production of tumor necrosis factor, or T.N.F., a protein that triggers inflammation in animals, including humans.

"We let it sleep for an hour, then took blood tests," he said. The bacterial toxin should have triggered rampant inflammation, but instead the production of tumor necrosis factor was blocked by 75 percent. "For me, it was a life-changing moment," Tracey said. What he had demonstrated was that the nervous system was like a computer terminal through which you could deliver commands to stop a problem, like acute inflammation, before it starts, or repair a body after it gets sick. "All the information is coming and going as electrical signals," Tracey said. For months, he'd been arguing with his staff, whose members considered this rat project of his harebrained. "Half of them were in the hallway betting against me," Tracey said.

Inflammatory afflictions like rheumatoid arthritis and Crohn's disease are currently treated with drugs — painkillers, steroids and what are known as biologics, or genetically engineered proteins. But such medicines, Tracey pointed out, are often expensive, hard to administer, variable in their efficacy and sometimes accompanied by lethal side effects. His work seemed to indicate that electricity delivered to the vagus nerve in just the right intensity and at precise intervals could reproduce a drug's therapeutic — in this case, anti-inflammatory — reaction. His subsequent research would also show that it could do so more effectively and with minimal health risks.

> 'There was nothing in the scientific thinking that said electricity would do anything. It was anathema to logic. Nobody thought it would work.'

Tracey's efforts have helped establish what is now the growing field of bioelectronics. He has grand hopes for it. "I think this is the industry that will replace the drug industry," he told me. Today researchers are creating implants that can communicate directly with the nervous system in order to try to fight everything from cancer to the common cold. "Our idea would be manipulating neural input to delay the progression of cancer," says Paul Frenette, a stem-cell researcher at the Albert Einstein College of Medicine in the Bronx who discovered a link between the nervous system and prostate tumors.

"The list of T.N.F. diseases is long," Tracey said. "So when we created SetPoint" — the start-up he founded in 2007 with a physician and researcher at Massachusetts General Hospital in Boston — "we had to figure out what we were going to treat." They wanted to start with an illness that could be mitigated by blocking tumor necrosis factor and for which new therapies were desperately needed. Rheumatoid arthritis satisfied both criteria. It afflicts about 1 percent of the global population, causing chronic inflammation that erodes joints and eventually makes movement excruciating. And there is no cure for it.

In September 2011, SetPoint Medical began the world's first clinical trial to treat rheumatoid-arthritis patients with an implantable nerve stimulator based on Tracey's discoveries. According to Ralph Zitnik, SetPoint's chief medical officer, of the 18 patients currently enrolled in the ongoing trial, two-thirds have improved. And some of them were feeling little or no pain just weeks after receiving the implant; the swelling in their joints has disappeared. "We took Kevin's concept that he worked on for 10 years and made it a reality for people in a real clinical trial," he says.

Conceptually, bioelectronics is straightforward: Get the nervous system to tell the body to heal itself. But of course it's not that simple. "What we're trying to do here is completely novel," says Pedro Irazoqui, a professor of biomedical engineering at Purdue University, where he's investigating bioelectronic therapies for epilepsy. Jay Pasricha, a professor of medicine and neurosciences at Johns Hopkins University who studies how nerve signals affect obesity, diabetes and gastrointestinal-motility disorders, among other digestive diseases, says, "What we're doing today is like the precursor to the Model T."

The biggest challenge is interpreting the conversation between the body's organs and its nervous system, according to Kris Famm, who runs the newly formed Bioelectronics R. & D. Unit at GlaxoSmithKline, the world's seventh-largest pharmaceutical company. "No one has really tried to speak the electrical language of the body," he says. Another obstacle is building small implants, some of them as tiny as a cubic millimeter, robust enough to run powerful microprocessors. Should scientists succeed and bioelectronics become widely adopted, millions of people could one day be walking around with networked computers hooked up to their nervous systems. And that prospect highlights yet another concern the nascent industry will have to confront: the possibility of malignant hacking. As Anand Raghunathan, a professor of electrical and computer engineering at Purdue, puts it, bioelectronics “gives me a remote control to someone’s body.”

Despite the uncertainties, in August, GlaxoSmithKline invested $5 million in SetPoint, and its bioelectronics R. & D. unit now has partnerships with 26 independent research groups in six countries. Glaxo has also established a $50 million fund to support the science of bioelectronics and is offering a prize of $1 million to the first team that can develop an implantable device that can, by recording and responding to an organ’s electrical signals, exert influence over its function. Instead of drugs, “the treatment is a pattern of electrical impulses,” Famm says. “The information is the treatment.” In addition to rheumatoid arthritis, Famm believes, bioelectronic medicine might someday treat hypertension, asthma, diabetes, epilepsy, infertility, obesity and cancer. “This is not a one-trick pony.”