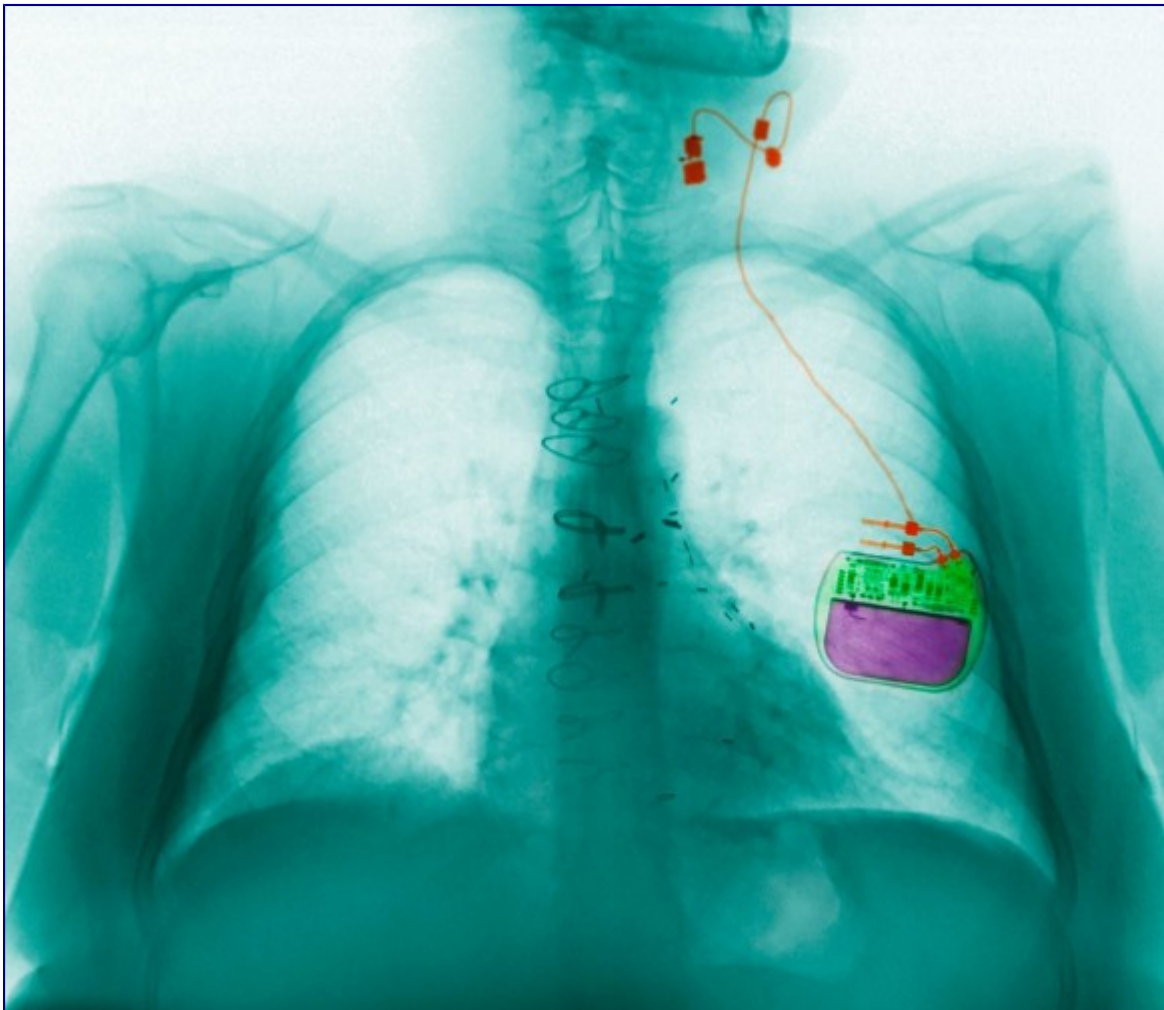


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- Date of Publication: 06.12.15.
- Time of Publication: 12:44 pm.

From Obesity to Epilepsy, One Nerve May Lead to Many Cures



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You've probably never heard of the vagus nerve before. But you really should. The longest of the twelve cranial nerves in the human body, the vagus nerve is promiscuous as far as biological entities go: It travels from the brain stem down all the way down into the abdomen, getting involved in lots of involuntary functions—keeping your heart pumping, your lungs breathing, and your intestines digesting. What happens in vagus most certainly does not stay in vagus.

The vagus nerve's winding, wandering path isn't just a useless anatomical oddity. Doctors can manipulate it to treat a whole range of human disorders, from epilepsy and depression to heart failure and diabetes. It even impacts processes relating to psychiatric health, the inflammatory system,

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movement, and the gut's microbiome. Medical and biotech researchers have spent much of the last two decades developing ways to stimulate the nerve to treat a number of those problems, and with a number of new therapies recently approved by the FDA—including one to treat obesity, of all things—it seems like the vagus nerve's time has finally come.

The best way to stimulate the vagus nerve, though, depends on what bodily system it's trying to change or suppress or activate. Here are the kinds of vagus nerve treatments researchers have been developing—and how promising they look.

Invasive Devices

Implanted devices are the most common form of vagus nerve stimulation (Houston-based company Cyberonics pioneered the approach, gaining FDA approval in 1997). A surgeon installs a pacemaker-like power generator under the skin, right below the shoulder, and tethers it to the vagus nerve. When the generator triggers an electrical signal, it travels through the nerve, activating an organ or biological process—which one depends on the kind of signal and how frequently it's sent.

The FDA has already approved this kind of vagus nerve implant for treating epilepsy and forms of depression that haven't responded to other treatments. In both instances, mild pulses of electricity stimulate the nerve during regular intervals. For epileptics, the electrical signals move up the brain stem, preventing the bursts of aberrant brain activity that lead to seizures—decreasing seizure rates from anywhere between 30 to 75 percent. In individuals with depression, the electrical signals trigger cortical regions that seem to affect mood and emotion, improving mental wellbeing in about 30 percent of depressed individuals (though, weirdly, researchers still don't know *exactly* what those brain changes look like and why they affect mood).

Many other companies are looking to tap into the vagus nerve to treat other kinds of health issues—like blocking hunger signals in diabetics and obese individuals, or controlling involuntary movement in people with multiple sclerosis. One of the most intriguing conditions being researched is heart failure. The vagus nerve runs right by the heart, controlling the rate at which it pumps blood. Cyberonics and other companies like Boston Scientific and BioControl Medical think they can keep the heart pumping by stimulating the nerve, without having to conduct a riskier operation that sticks a pacemaker right by the heart itself—but so far, results from clinical trials don't show that it's any better than a more traditional implant.

Of course, the biggest drawback to an implantable stimulator is that patients need to undergo surgery, and live with an implant in their body the rest of their lives (or for as long as they require treatment). And for that reason, many other researchers are trying to develop methods that can stimulate the vagus nerve without putting patients under the knife.

Noninvasive Devices

A noninvasive device would go a long way to develop vagus nerve stimulation as a common form of

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therapy like an over-the-counter medication—not just a special treatment for individuals with few other options. The major player developing that kind of stimulator is ElectroCore Medical, a New Jersey-based startup that wants to treat headaches and recurring migraines.

Their design is simple. When you feel your head beginning to throb, you press their portable device against the lower left side of your neck—where the vagus nerve passes through—for a few minutes. The device delivers small, very fast pulses of voltage capable of traveling through the skin and muscle and stimulating the vagus nerve, and higher settings can be applied for more debilitating headaches.

ElectroCore's device has already been approved for headaches and migraines in Europe, but FDA approval here in the US will require more rigorous testing. Beyond that, the company hopes to find out if the device can treat other illnesses as well.

Acute Intervention

Stimulating devices—implanted or not—make sense for long-term ailments. But vagus nerve stimulation could also be good for treating a temporary problem like inflammation, and for that, you would want a faster-acting intervention.

Inflammation is a function of the immune system—it's the way the body tries to get a grip on injuries and acute infections. The vagus nerve helps keep this process from going haywire by calling for the release of anti-inflammatory signals from immune cells. But if left unchecked, inflammation can cause even more damage to surrounding tissue and organs, leaving the body at risk of acquiring an infection.

Surgeons at the University of California, San Diego are currently testing the effects of vagus nerve stimulation in decreasing inflammation in burn victims. They've already tested direct stimulation—by applying an electrode to the nerve via a small surgical incision made on the neck—on rodents who have sustained burn injuries. The results have shown a significant decrease in intestinal inflammation.

But Todd Costantini, one of the researchers on the project, says the ideal way to achieve the same effects in humans would be through a pharmacological agent that can be injected or ingested. The research on that front is still in its infancy, and the mechanism by which a drug could target the vagus nerve is not fully fleshed out yet. But Costantini hopes he and his colleagues can develop something that can be delivered to someone at the scene of an emergency or en route to the hospital. Turns out it's not always a bad thing to hit a nerve.