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Electroceuticals spark interest

Industry and academia invest in treating diseases by delivering electrical charges to nerves.

- Sara Reardon

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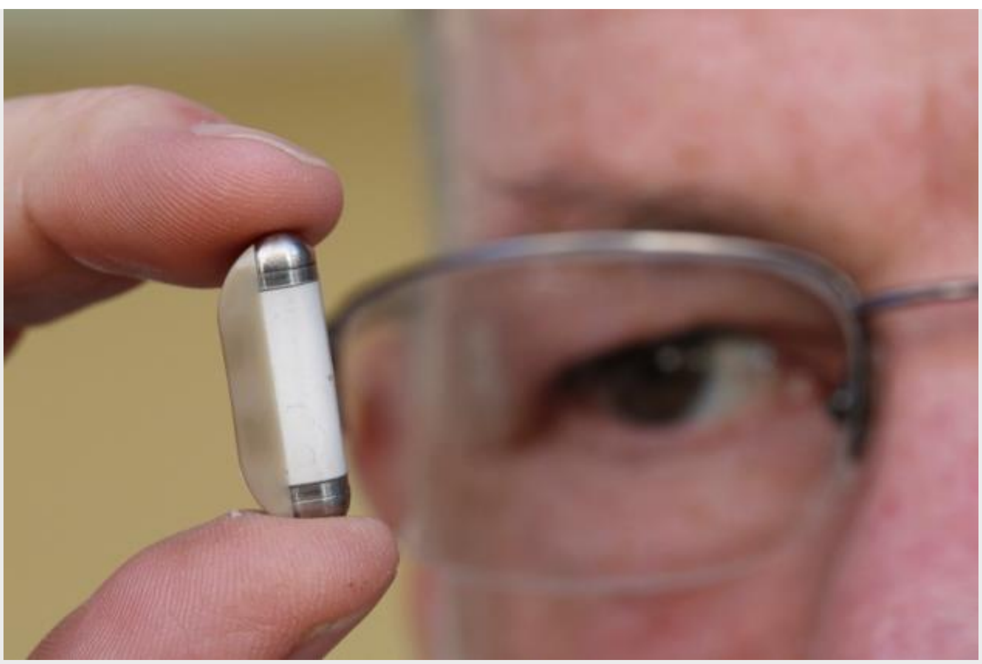
Electroceutical Medicine

Electroceutical are medicines that use specifically targeted electrical, sound, magnetic, photonic or other energy impulses to engage a specific biological and/or physiological function where the electrical energy is used to initiate a biological change. Electroceutical are medicines that stimulate hormone or enzyme activity or correct diseased or aberrant process without drugs or SINthetic chemicals.



Patrick T. Fallon

A microregulator implant made by SetPoint Medical is designed to stimulate nerves to reduce inflammation.

When drugs can’t coax cells in the pancreas to produce insulin, or loosen arteries to reduce blood pressure, a well-placed jolt of electricity might do the trick. Spurred by decades of success with pacemakers and cochlear implants, and by advances in miniaturized technology, interest is surging in ‘electroceuticals’ — bioelectronic implants that stimulate nerves to treat disease.

Next week, the US National Institutes of Health (NIH) will announce a US$248-million effort to map the body’s electrical wiring and develop such devices. Pharmaceutical giant GlaxoSmithKline (GSK) has already set up a similar programme — and biotechnology companies are on the verge of bringing products to market.

On 1 May, the US Food and Drug Administration (FDA) approved a device by Inspire Medical Systems of Minneapolis, Minnesota, that stimulates airway muscles to treat sleep apnoea by regulating breathing while a person sleeps. And on 17 June, an FDA advisory committee recommended that the agency approve a weight-control device from EnteroMedics in St Paul, Minnesota. Implanted between the oesophagus and stomach, it stimulates the vagus nerve to make a person feel full.

Scientists predict that there are many more devices to come. “The nervous system is criss-crossing our viscera to control many aspects of our organ function,” says Kristoffer Famm, head of the bioelectronics unit at GSK in London. Rather than targeting cells with a drug, he says, treatments could send an electrical pulse to a major nerve to alter the commands an organ receives, and thereby control its function.

Such treatments could be more precise than pharmaceuticals, says Brian Litt, a bioengineer at the University of Pennsylvania in Philadelphia. In autoimmune diseases, for instance, it may make sense to place an electroceutical device on a well-chosen nerve rather than to blast the whole immune system with a drug. Disorders that involve targets such as the bladder, whose function is controlled by several nerve inputs, and the vagus nerve, which has a role in numerous systems including the inflammatory response and appetite, also seem ripe for electrical interventions.

“Traditional approaches of drug discovery and swallowing a pill will not be the optimal way to treat a number of diseases,” says Warren Grill, a biomedical engineer at Duke University in Durham, North Carolina, who studies electrical control of bladder function.

With that in mind, last December GSK announced a $1-million prize for the first team to develop a miniaturized, implantable device that can read specific electrical signals and stimulate an organ to perform a specific function reliably for 60 days (K. Famm*et al*. *Nature* **496,** 159–161; 2013). The company has spent $50 million on in-house electroceutical research, and it is also funding a consortium of scientists at 25 universities to develop devices that can be made available to the broader research community. Famm says that the researchers are working on electroceuticals for 20 different disorders that range from cardiovascular disease to rheumatoid arthritis and cancer. “It’s a fascinating time, although we don’t expect all those organs to be a slam dunk,” he says.

Bioelectronic implants seem promising, but it is often unclear why they work. "Right now, a lot is based on phenomenology," says Kip Ludwig, director of neural-engineering programmes at the US National Institute of Neurological Disorders and Stroke in Bethesda, Maryland. "You put an electrode in the body, you stimulate, and you get an effect."

The NIH electroceuticals project, tentatively called Stimulating Peripheral Activity to Relieve Conditions (SPARC), plans to bridge the knowledge gap by taking a step backwards and focusing on the mechanisms that underlie electrical control of organ systems. Its first grants will be awarded in early 2015. Over the next six years, the agency hopes to map the nerves and electrical activity of five yet-to-be-decided organ systems and then develop electrode devices that can attach to the nerves and maintain high-resolution recording and stimulation interfaces with them for decades without causing damage.

The most challenging task will be teasing apart the hundreds of signals that run to and from each organ. The goal is to build devices that target only the signal that elicits a desired effect, and not those that could alter functions in other parts of the body, says Litt. It is a mammoth task, he adds: "It's like putting a device across a highway, and trying to figure out, by looking at the cars passing, which will get off at which exit."

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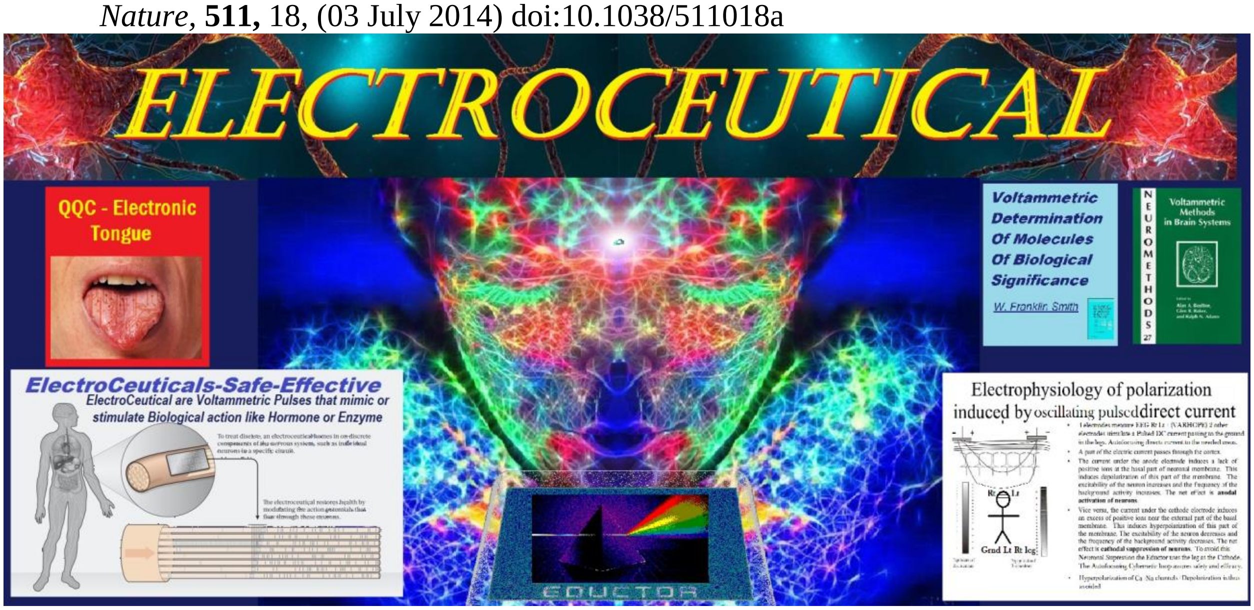

One day, in the not *too* distant future, you might not recognize the **pharmaceutical industry**…

Right now, pharmaceutical firms develop drugs that interact biochemically with our bodies in order to treat various diseases and conditions. But that's changing…

A number of pharmaceutical companies will eventually transform into bioelectronics companies. Their treatments will consist of tiny implantable devices that "speak" the body's electric language.

Think of it as a type of technology similar to a heart pacemaker. But much, *much* more advanced.

The Brave New World of Electroceuticals

Welcome to the brave new world of neuromodulation and electroceuticals. It's a world where neural signal modulation will be the treatment path followed by tomorrow's doctors, not drugs.

Most electroceuticals will be about the size of a grain of rice. The devices will be attached to peripheral nerves and will modulate neural signals.

This will be a quantum leap from current disease treatment methods using drugs, which are actually very blunt instruments. And we all know about the numerous side-effects drugs can cause…

Whereas regulating the electrical firings of neural circuits can be far more precise and without the nasty side-effects. So says Kristoffer Famm, Vice President of Bioelectronics at **GlaxoSmithKline Plc**(**GSK**). As he told the *Financial Times*, "The nervous system is a fundamental control system in biology."

And the nervous system is where scientists are exploring new frontiers. Prime early opportunities bioelectronics research is focusing on metabolic, cardiovascular, and inflammatory disorders.

Bioelectronics Research

One prime area of research for bioelectronics is the brain and epilepsy. Epilepsy is directly caused by an electrical malfunction of the brain. This common neurological disease affects more than 50 million people worldwide. And conventional drugs aren't really that effective in combating it.

However, most current bioelectronics research is focused on the electrical language of peripheral nerves outside the brain and spinal cord. It's these nerves that influence the function of every organ in the body.

DARPA (the Defense Advanced Research Projects Agency) is involved in the field through its $79 million Electrical Prescriptions (ElectRx) initiative.

The head of the program, Doug Weber, spoke to the *Financial Times* about the importance of the research into peripheral nerves:

The peripheral nervous system is the body's information superhighway, communicating a vast array of sensory and motor signals that monitor our health status and affect changes in brain and organ functions to keep us healthy.

The aforementioned GSK is the leader in electroceutical research. It has over 50 research collaborations on bioelectronics around the globe. In 2013, GSK set up the $50 million Action Potential Venture Capital Fund and has invested in five start-ups to date.

One company GSK invested in is SetPoint. It's developing an implantable device that stimulates the vagus nerve in the neck with electrical impulses. The goal is to counter the inflammation caused by rheumatoid arthritis and Crohn's disease.

Another start-up, ElectroCore (not affiliated with GSK), is taking a different route with electroceuticals. It thinks treatments can be delivered through the skin. It wants to treat migraine headaches by stimulating the vagus nerve with electrical impulses to the neck. The goal is control glutamate, which has been linked to migraines.

The Future Is Here

In a way, the future is already here. The Food and Drug Administration (FDA) approved the use of some electroceuticals a few years ago.

The first example is Inspire Medical Systems' treatment of sleep apnea by the implantation of a device that stimulates the airway muscles.

A second example is a treatment for morbid obesity from **EnteroMedics Inc.** (**ETRM**). This implantable device stimulates the vagus nerve to make a person feel full. However, results for the weight control device have been mixed.

The future for electroceuticals, however, looks bright.

GSK's Famm compares the potential of bioelectronics in medicine to what Apple did for phones.

We likely won't see most of that potential until perhaps the end of the decade. Most current research is still at the animal experimentation stage.

For the use of electroceuticals to become widespread, technology still needs to advance. Improvements need to made in power sources, for example. Wireless rechargeable batteries that last for decades would be ideal.

When such advances do occur, it will mark a complete transformation of the pharmaceutical industry.

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