Electrical Stimulation and Pacing for Digestive Disorders in Adults and Children: A Status Report

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Background

Nerves and muscles are excitable. They respond actively to an electric stimulus, and electrical current contributes to that property. In nerves, current moves along the cell membrane with messages to other nerves or other tissues. In muscle, electrical currents signal the muscle to relax or contract. The brain is made up of nerve cells, and the brain's sum of electrical activity is measurable as a graphic recording – the electroencephalogram, or EEG. When the brain is normal, the EEG is normal, but if someone has a stroke or a seizure, for example, the EEG is abnormal. The heart is made up of mostly muscle and a little nerve. The sum of the heart electrical activity is called the electrocardiogram, ECG, or EKG. When the heart is normal, the ECG is normal. If the heart has abnormal circuitry or there is a heart attack, for example, the ECG is abnormal.

A few years ago, gastroenterologists learned that the stomach has two kinds of electrical activity: slow waves and spikes. Slow waves are continuous undulating rhythms of electrical charges – polarization and depolarization – due to opening and closing of ion channels (molecular "gates" that regulate nerve signaling) on the smooth muscle membrane. Spikes are rapid changes in electrical charges (membrane depolarizations) during the most depolarized part of the slow wave. Spikes are necessary for muscle contraction. Gastric slow waves in the stomach normally cycle three times every minute. When something causes nausea, slow waves become disorganized.

In the laboratory slow waves are measured in individual cells with microelectrodes, or by electrodes that sum the signals. In humans, electrodes may be stitched onto the inside or outside lining of the stomach. Recently researchers learned how to measure slow wave activity using electrodes on the skin, identical to recording an ECG, except that the electrodes are placed over the stomach instead of over the heart. Patients who have gastric nerve problems have abnormal slow wave frequencies. For example, instead of having the normal gastric electrical signal of 3 cycles per minute, patients with gastric paralysis, or gastroparesis, have slow wave frequencies that are too fast (tachygastria) or too slow (bradygastria). When slow waves are not in the correct rhythm, spikes do not occur when the slow wave is at its most depolarized. Hence, the needed signaling from nerve to muscle (electro-mechanical coupling) does not occur, smooth muscle does not contract, and normal gastric emptying of a meal cannot proceed.

In the special situation when nerves that signal the heart to beat regularly are not working, cardiologists place a pacemaker into the heart. The pacemaker is a wire attached to an electrical battery. The pacemaker is programmed to deliver electric current to the heart at intervals, signaling it to contract at the correct times.

In the last two decades researchers from other specialties involving nerves and muscles began experimenting with electricity to correct abnormalities in nerve or muscle in other organs, such as the urinary bladder and gastrointestinal tract. The gastrointestinal tract has nerves and muscles from top to bottom, and there are many reasons that excitable tissues of the gastrointestinal tract may be damaged, such as infections, diabetes, and inflammatory bowel disease. The result of damage to muscle or nerve of the gastrointestinal tract may be gastroparesis (inability of the stomach to empty its contents into the small intestine), or chronic intestinal pseudo-obstruction (inability of the intestines to move its contents through the intestines for nutrient absorption or waste elimination). Gastroparesis is common, but often difficult to treat. Chronic intestinal pseudo-obstruction is rare, and even more difficult to treat than gastroparesis. Researchers investigating abnormal gastric motor function thought that when nerves within the stomach are not working properly, a pacemaker placed into the stomach might work in a manner analogous to the cardiac pacemaker.

Gastric electrical pacing and electrical stimulation

Two decades ago at the University of Virginia and Mayo Clinic, the first attempts to pace the stomach and intestines got started. First in animals and then in humans, there was modest success. However, the technology was cumbersome, and clinical application seemed distant.

Gastroparesis is a chronic disorder of gastric (stomach) motility, characterized by delayed emptying of solid foods without evidence of an anatomic obstruction. Patients with gastroparesis suffer from chronic nausea, vomiting, and weight loss. Gastroparesis occurs when the nerves or muscles are not working right. Gastroparesis seemed the best target for exploring how pacing might work for two reasons: there are a lot of patients with gastroparesis, and the stomach, like the heart, is a globular (spherical) organ, compared to the tube-like esophagus, small intestine, and large intestine. The shorter distances from start to finish gave hope that an electrical signal would not decrease in strength as it moves along.

Pacing the stomach by entraining the gastric slow wave to try to help normalize stomach motility in patients with gastroparesis is underway at the University of Kansas Medical Center. This research study enrolled the first patients at the beginning of 2006. Volunteers with gastroparesis unresponsive to all other treatments undergo surgery to implant electrodes in two places on the stomach surface. Electrical wires from the electrodes come out through a small hole on the abdominal wall. Patients must wear a fanny pack that holds a rechargeable battery that provides the energy for high energy pulses that are required to regulate the slow waves, activate electro-mechanical coupling, and start the stomach muscle working. Patients hook up during and after meals.

About ten years ago, understanding the effects of electricity on gastrointestinal tissue entered a second phase of renewed interest. Working with engineers from Medtronic, a consortium of investigators examined a role for electrical stimulation, not pacing, on gastroparesis. Pacing the gut, like the heart, requires high energy, low frequency electrical pulses. In contrast, electrical stimulation with the Medtronic pulse generator placed under the skin delivered low energy, high frequency short pulses to electrodes secured into the muscle on the greater curve of the stomach. No external wires are needed, everything is implanted under the skin. There is enough energy in the battery to last 7 or 8 years using the standardized stimulation parameters.

The gastric electrical stimulator (GES) was approved by the FDA in March 2002. Centers with special interest in gastroparesis have placed most of these devices. The device reduces nausea, vomiting, and symptoms of gastroparesis without changing gastric motility. Patients with gastroparesis caused by nerve damage associated with diabetes (diabetic neuropathy) have an 80% response rate compared to a variable response rate in patients with gastroparesis from all other causes. Centers with special interest are prospectively recording the results of all the patients with GES. Complications, such as infections or device movements, have been uncommon. Only about 5 in 100 devices are removed because of complications. Over 2,000 devices have been placed in adults with gastroparesis. The University of Kansas Center for GI Nerve and Muscle Function in Adults and Children currently has the world's largest single center experience with 180 devices implanted, including the youngest patient to have this surgery. He is a 7 year old child with coalescing cyclic vomiting syndrome. His symptoms improved just after the device was placed, and it continues to relieve symptoms over a year following placement.

Obesity

Obesity is an epidemic health threat. There are many solutions for obesity, but it helps to have choices. Because investigators normalized slow waves and reduced nausea with electrical current, would it be possible to use different currents to purposely slow gastric emptying or induce early feeling of fullness (satiety), nausea, or discomfort to treat obesity? Trials to evaluate disorganizing gastric electrical rhythms to treat obesity have been completed in Europe and the USA. At this time, data suggest that investigators have not yet discovered the proper electrical parameters, electrode positioning, and physiologic targets to achieve meaningful and sustained weight loss.

Conclusion

Electrical stimulation is used for treating abnormal function in a variety of excitable tissues: brain to treat depression, vagal nerve to treat seizures, spinal cord for pain, transcutaneous (through the skin) sites for pain and headache, deep brain for Parkinson's disease, sacral for urinary and fecal incontinence, and cardiac for heart arrhythmias. It should come as no surprise that there may be a role for electrical pacing and stimulation in the gastrointestinal tract. There are many future research avenues. For example Dr. Jiande Chen's laboratory, at the University of Texas at Galveston, has placed multiple electrodes into dog small intestine, and showed that pacing from one electrode to another induces peristalsis and propagation of the intestinal contents. In another laboratory, Drs. Soffer and Mintchev have done the same with dog colon. These data suggest that electrical pacing may be applied to the intestines as well as the stomach, and provide a novel treatment for chronic intestinal pseudo-obstruction and severe constipation, respectively.

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