INVESTIGATOR HIGHLIGHTS

Ken Gustafson, PhD
VA Office of Rehabilitation Research & Development
Merit Review

Svetlana Pundik, MD, MSc
VA Office of Rehabilitation Research & Development
Merit Review

John Chae, MD
MetroHealth System
Vice President of Research

Aasef Shaikh, MD, PhD
Cleveland VA Movement Disorders Center
‘VA Parkinson’s Consortium’ site designation

Bolu Ajiboye, PhD
7th Annual Brain-Computer Interface Conference
Graz, Austria
Keynote Speaker

Kevin Kilgore, PhD
National Institutes of Health, National Institute of Biomedical Imaging and Bioengineering
R01 Award

Hunter Peckham, PhD and Megan Moynahan, MS
National Institute of Neurological Disorders and Stroke (NINDS)
Cooperative Research to Enable and Advance Translational Enterprises (CREATE) for Biotechnology Products

Book Chapters

John Chae, MD and Rich Wilson, MD wrote the chapter, ‘Comprehensive Pain Management in the Rehabilitation Patient’ for the textbook Percutaneous Peripheral Nerve Stimulation for the Treatment of Acute and Chronic Pain, by Brian Ohlendorf and Stuart A. Grant, and published by Springer International Publishing in 2017.

Rich Wilson, MD wrote the chapter, ‘Rehabilitation after Pelvic Ring Injury’ in the textbook Postoperative Orthopaedic Rehabilitation, by Andrew Gree and Roman Hayda, and published by Lippincott Williams & Wilkins in 2017.

BrainGate2 research by Bolu Ajiboye, PhD and Robert Kirsch, PhD was prominently featured in chapter nine of The Performance Cortex: How Neuroscience Is Redefining Athletic Genius, by Zach Schonbrun, and published by Dutton in 2018.
Acute and chronic pain affect at least 100 million U.S. adults and cost the nation up to $630 billion in medical treatment and lost productivity annually, according to the National Academy of Medicine. There are many treatment options for pain management, including medication, neuromodulation, local anesthetics and surgery. Researchers at the Cleveland FES Center are developing innovative solutions focused on electrical nerve blocks – essentially targeting nerves that send the pain signal to the brain and blocking the nerves from sending that signal. 

“Pain is one of the largest disease groups in the U.S. It’s larger than heart disease and cancer combined,” says Tina Vrabec, PhD, a member of the research faculty in the Department of Biomedical Engineering (BME) at Case Western Reserve University (CWRU). “Part of what drives us forward in our research is thinking about the sheer size of the population we can benefit and what our impact can be.”

For the past two years, Vrabec and Niloy Bhadra, MD, PhD, an investigator at the Cleveland FES Center and a research assistant professor in BME at CWRU, have partnered with medical technology company Halyard Health to create cutting-edge electrical nerve block solutions. Most recently, the work has focused on minimally-invasive direct current nerve blocks, typically delivered percutaneously via a small catheter containing a conductive fluid that delivers the stimulation.

“Products based on our electrical nerve block would fit well within Halyard Health’s existing products for pain after surgery and chronic pain relief,” says Kevin Kilgore, PhD, an investigator at the FES Center. “The overarching goal is to move our ideas into clinical testing and eventually onto the market for treatment of pain.”

Moving from High-Frequency to Direct Current Blocks

The project with Halyard Health is the latest in nearly two decades of research on pain management conducted by Bhadra and Kilgore, who began studying electrical nerve blocks to get spastic muscles – such as those in stroke or multiple sclerosis – to relax and improve function. “As...
“Part of what drives us forward in our research is thinking about the sheer size of the population we can benefit and what our impact can be.”

— Tina Vrabec, PhD
our research into nerve block started showing promise, it became apparent that our technique might be used to block any nerve, including pain fibers,” says Kilgore.

The researchers initially concentrated on delivery of high-frequency alternating current waveforms to produce reversible nerve blocks. Neuros Medical Inc., a Cleveland-based company, licensed the FES Center’s patent for chronic amputation pain. With the company’s Altius® System, an electrode is placed around a peripheral nerve, then a small implanted generator sends a high-frequency signal to the electrode to block the pain signal.

The basic difference between high-frequency (HF) blocks and the newer direct current (DC) blocks is in the frequency of the waveform. With HF blocks, the current cycles positive and negative approximately 10,000 times per second. That cycle occurs about once per minute for DC blocks. “We refer to it as ‘direct current’ because the cycle time is so slow that the body reacts to it as if it were unchanging,” says Kilgore.

**Customizing Pain Solutions for Specific Applications**

Vrabec and Bhadra lead a team of 10 researchers on the collaborative pain management project funded by Halyard Health. The interdisciplinary team includes people with expertise in biomedical, chemical and electrode engineering. They have conducted a lot of basic research for the past two years, studying various kinds of blocks as well as different electrodes.

The basic research involves bench testing – “lots of nuts-and-bolts engineering on electrochemistry, device building and mechanical challenges,” says Vrabec. Once the devices are evaluated, then the team tests them in biologic studies to determine the block’s effectiveness and get parameters for each of the interventions.

The researchers are pursuing a wide array of solutions because pain varies depending, for example, on where it’s located in the body and whether it’s acute or chronic. “One of the big pushes in medical care right now is for customization and patient-specific interventions,” says Vrabec. “We have a wide toolbox at our disposal – a bunch of different types of electrodes, from implantable to surface electrodes, and different waveforms that may work for some applications better than others. Our systems need to be specific to the requirements [the medical community] is trying to address.”

**Tapping into the Benefits of Direct Current Blocks**

DC blocks have several advantages over other pain management options, such as medication and local anesthetics. One of the biggest benefits is their rapid onset and reversal. “The problem with using drugs is the time needed to control the pain can be anywhere from 30 minutes to six hours,” says Bhadra. “In addition, drugs are non-specific, so they will not only kill the pain, but also have many side effects. Then, when the pain stops, it takes time to come down from effects of the drug. With DC blocks, we can reverse the effects almost immediately.”

DC blocks also can be graded, offering a total block, 90 percent block, 80 percent block and so on. For acute pain, you probably want a complete block. “But when you are tackling pain with peripheral nerve, you also affect motor systems,” says Bhadra. “So you can grade the DC block and still allow the muscle to function.”

Think about novocaine use for dental work: Patients have to wait until their mouths are numb to begin the procedure, then when it’s over, the novocaine often takes hours to wear off. “Imagine how great it would be to have an option that only takes the pain away without losing functionality of your mouth,” says Vrabec.

**Transferring Solutions from the Lab to the Market**

Investigators at the FES Center are excited at the prospects for direct current nerve blocks, some of which are undergoing in vivo biologic studies in tandem with
Halyard Health. “The bottom line is that no one else has ever done this,” says Bhadra. “We are the first group to show you can safely perform DC blocks without killing the nerve.”

Recently, the group has begun testing combinations of surface electrodes and implantable systems, as well as solutions that utilize both HF and DC nerve blocks. It’s all part of the extensive toolbox that Vrabec referenced. And while the tools may vary, the primary goal of all electrical nerve blocks is the same – to relieve pain.

“Imagine that you could have a local anesthetic like lidocaine, but it came with a switch that would allow you to turn it on or off whenever you wanted,” says Kilgore. “That is the innovation we are working on. If we can make this technique reliable and safe, it will have a lot of different applications.”

From left: Kevin Kilgore, PhD, Niloy Bhadra, MD, PhD, Tina Vrabec, PhD perform bench testing to study electrochemistry, device building and mechanical challenges.
Anthony DiMarco, MD, Principal Investigator, and Krzysztof Kowalski, PhD, Co-Investigator, are among a team of researchers at the Cleveland FES Center that is combining two systems to offer complete restoration of respiratory muscle function to subjects with spinal cord injury (SCI). Results of an interventional clinical trial demonstrate that a spinal cord stimulation system to restore cough can be used safely and effectively in conjunction with a diaphragm pacing system to restore breathing.

Many individuals with SCI develop respiratory compromise and require mechanical ventilatory support. However, individuals with ventilator-dependent tetraplegia can often be offered an alternative method of ventilatory support through diaphragm pacing, which provides a more natural form of breathing. “We have also demonstrated that diaphragm pacing could be achieved via a less invasive method i.e. laparoscopically placed intramuscular diaphragm electrodes. This method has been successful in liberating thousands of individuals from mechanical ventilation,” says Dr. DiMarco.

A second system has been developed at MetroHealth Medical Center to restore an effective cough to individuals with SCI, thereby helping to reduce the risk of aspiration and the development of respiratory tract infections including pneumonia. “We developed the first method in the world by which we can activate expiratory muscles – abdominal and lower rib cage muscles, using minimally invasive techniques– to produce an effective cough,” says Dr. Kowalski. The initial system was implanted surgically, with disc electrodes placed on the dorsal surface of the spinal cord via laminectomy. Drs. DiMarco and Kowalski have subsequently developed a minimally invasive method using wire electrodes that are inserted percutaneously through needles, then advanced to the dorsal spinal cord under fluoroscopic guidance. Research subjects utilize a stimulator to produce several different cough efforts ranging from light to strong.
An interventional clinical trial conducted by the research team shows the efficacy of using the two systems in tandem. “Subjects can employ diaphragm pacing to restore breathing and also generate an effective cough by simply pushing a button. The project has been very rewarding. We see so many subjects who are very pleased with the system and have achieved significant clinical benefit.” says Dr. DiMarco.

“Being a part of this research trial has made me feel great for not only my own health, but helping to improve the lives of others as well.”

- David Powers | Research Participant
In September, Governor Chris Christie, Secretary David J. Shulkin, former Representative Patrick Kennedy, and Counselor to the President Kellyanne Conway, visited the Cleveland FES Center BrainGate2 program.

Benjamin Deady, Director of the District Communications Group for the VA Pulse, toured FES labs.

Thomas G. Bowman, Deputy Secretary of Veterans Affairs, visits the Cleveland FES Center Stroke trial, *Contralaterally Controlled Functional Electrical Stimulation*.

From left: Sue Fuhrer, Director of the Louis Stokes Cleveland VA Medical Center, leads a tour through the Cleveland FES Center labs for Jake Leinenkugel, Senior White House Advisor to the Department of Veterans Affairs, and John Wolf Wagner, Principal Deputy Assistant Secretary for Public and Intergovernmental Affairs at the US Department of Veterans Affairs.
SPREADING THE WORD

Paralyzed Veterans of America Wheelchair Games, Buckeye Chapter
FES Center operations supported the 7th Annual PVA Wheelchair Games, Buckeye Chapter at SPIRE Institute in Geneva, Ohio.

Gordon Research Conferences
Jeffrey Capdona, PhD was the 2018 co-chair of the Neuroelectronic Interfaces GRC entitled “Beyond Feasibility – Bridging the Gap in Neuroelectronic Interfaces,” in Galveston, Texas.

Bass Neurosurgery Symposium: The Technologies of Neurorestoration
Robert Kirsch, PhD gave a lecture entitled, “Restoring Function After Spinal Cord Injury Using Direct Brain And Nerve Stimulation” at the Bass Neurosurgery Symposium in Dallas, Texas.

Minnesota Neuromodulation Symposium
Andy Cornwell, PhD represented the Cleveland FES Center at the 2018 Minnesota Neuromodulation Symposium.

North American Neuromodulation Society
The Cleveland FES Center networked at 2018 NANS, the world’s largest meeting in the field of neuromodulation, in Las Vegas, Nevada.

Design of Medical Devices Conference
Andy Cornwell, PhD attended the 2017 DMD Conference in Minneapolis, Minnesota to see new perspectives and innovations in medical device design.

Student Mentorships
Cleveland FES Center welcomed internship students from Laurel School, Mentor High School, Padua Franciscan High School, and Valley Forge High School. While we continue contributing to the medical research in neuroscience, we help the next generation explore their future career paths.

FES Institute

SUPPORT

Thank you to the FES Institute for the generous partnership support to FES Center educational and outreach programs.