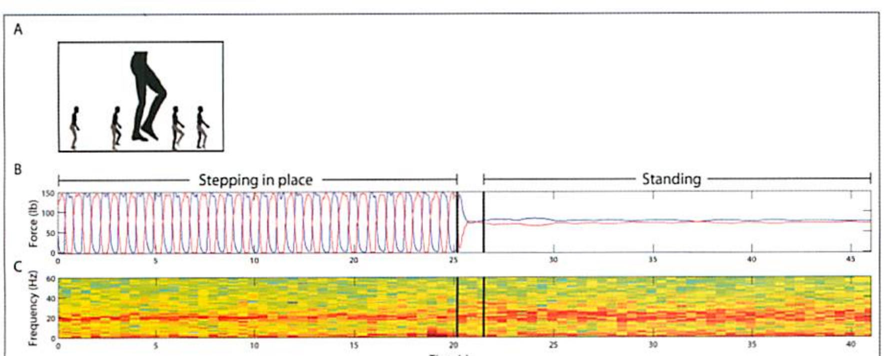
# The Brain Pacemaker

Helen Bronte-Stewart, MD, MSE, neurologist, physicist and engineer, epitomizes the scientific pursuit to link quantitative data and qualitative observations. When she established the Motor Control and Balance Laboratory at Stanford over 13 years ago, little was known about how brain signals affect movement.

Now, in an equipment-for-data collaboration with Medtronic Inc, she is one of the first to test a therapeutic innovation for patients with such disorders: a sensing neurostimulator coupled to an implanted deep brain stimulation (DBS) device. This feedback device allows her team to record real-time brain signals and quantitative kinematic measures as a patient *moves freely in the clinic*. These real-time data help physicians and ultimately the device itself, independently, finely tune electrical parameters to optimize patients' movements, minimize side effects and prolong the battery life. This is "the next step toward the demand brain pacemaker," says Dr. Bronte-Stewart, the John E. Cahill Family Professor of Neurology and Neuroscience.

"We use electrophysiology speak to characterize rhythms and electrical profiles of voltage, pulse width and frequency, which mean to us milligrams of a drug or dosing frequencies," she adds. "But it's just electronic and not in pill form. For us the central question is how can we refine and optimize DBS if we can't record and quantify the electrical output responses or signals that are altered by the DBS device?"



Schematic diagram (A); Concurrent ground reaction forces (B) and STN LFP time-frequency spectrogram (C) of a Parkinson's disease subject: stepping in place and standing still. Note the narrower band of beta synchrony during stepping versus standing still.


Jaimie Henderson, MD and Helen Bronte-Stewart, MD

Affectionately known to colleagues as the "data monster," Dr. Bronte-Stewart has for more than a decade produced answers. The first step was to establish quantitative metrics that identify the unique characteristics of movement disorders. Her groundbreaking study in 2000 showed that the cardinal signs of Parkinson's disease, bradykinesia, temporal abnormalities, variability, freezing behavior and tremor, could be tracked using a MIDI computer-interfaced keyboard. Her lab has now engineered a keyboard with a finer resolution in the measurement of timing, velocity, pressure, and position of finger movements.

Dr. Bronte-Stewart has also used computerized dynamic posturography (CDP) to quantify different aspects of balance in people with movement disorders. This is a significant advance over subjective clinical rating scales. Using CDP her team has developed the first metric of freezing-of-gait in Parkinson's disease and has shown that even when patients' feet seem "frozen" their brains nonetheless send alternating weight-shifting signals to their feet, though not strong enough to actually lift them. Her measurements of limb movement revealed that finger movement data sufficiently reflected all other symptoms. In patients undergoing DBS, she and colleague Jaimie Henderson, MD, the John and Jene Blume — Robert and Ruth Halperin Professor of Neurosurgery and director of stereotactic and functional neurosurgery, routinely use her finger-tracking keyboard in the operating room as a diagnostic tool. This new brain signal sensing device

*continued on page 18* ▸

**Jamshid Ghajar, MD, PhD**

*Clinical Professor of Neurosurgery*

Dr. Ghajar is a foremost expert in traumatic brain injury. At Stanford he is director of the Stanford Concussion and Brain Trauma Center. He has served as President of the Brain Trauma Foundation since 1995 and was previously Chief of Neurosurgery at The Jamaica Hospital-Cornell Trauma Center in New York from 1989–2014. He has received multiple patents for brain neurosurgical tools and cognitive assessment devices. He is a leading grantee and advisor for the Department of Defense.

**Casey Halpern, MD**

*Assistant Professor of Neurosurgery (As of September 1, 2014)*

Dr. Halpern received his neurosurgical training at the University of Pennsylvania. His specialty is the treatment of functional disorders, including movement disorders, epilepsy, chronic pain, and spine disease. He is particularly interested in developing clinical trials that expand indications for deep brain stimulation (DBS). Dr. Halpern's laboratory research investigates the therapeutic role of DBS that targets the brain's reward circuitry. His studies could lead to a better understanding and possible treatment for relapse behavior common to many neurologic and psychiatric conditions, and even obesity.

**Josh Levin, MD**

*Clinical Assistant Professor, Physical Medicine & Rehabilitation Division, Departments of Orthopaedic Surgery and Neurosurgery*

Dr. Levin is a triple board certified physiatrist who specializes in the diagnosis and non-surgical treatment of spine disorders. He is a part of Stanford's growing comprehensive spine team, and his practice includes interventional spine procedures and EMG. His research interests include evaluating subsets of patients who may benefit from percutaneous treatments of the facet joints, evaluation of novel objective outcome measures in the treatment of spine and musculoskeletal disorders, and investigating treatment options for discogenic pain.

**Jessica Little, PhD**

*Clinical Assistant Professor of Neurosurgery*

Dr. Little is a clinical psychologist with an extensive background in international and multi-site research. As director of Clinical Research and Operations at the newly-formed Stanford Concussion and Brain Trauma Center she is working to prioritize interdisciplinary research collaboration at Stanford and to develop an infrastructure for large-scale, evidence-based clinical trials. Her current research focuses on mild traumatic brain injury and the intersection of neuromotor technology and cognitive assessment.

**Peter Tass, MD, PhD**

*Consulting Professor of Neurosurgery*

Professor Tass is a computational neuroscientist with extensive translational experience. He directs the Institute of Neuroscience and Medicine-Neuromodulation (INM-7) at Jülich Research Center (Germany) and developed FDA and CE mark approved Medtech stimulation devices. His approach aims at unlearning abnormal synaptic connectivity and, hence, inducing long-lasting therapeutic effects. He has joined the department of neurosurgery as a consulting professor working primarily in the area of neuromodulation for the treatment of tinnitus, Parkinson's disease, epilepsy, and pain.

*The Brain Pacemaker continued* ▸

is exciting for both what it can reveal and where it can be utilized. It links quantitative brain signals to Dr. Bronte-Stewart's metrics for tremor, bradykinesia and freezing of gait by sensitively and instantaneously reporting a patient's response to a physician's tweaks of a pacemaker's voltage. Diseases can be diagnosed more precisely and detected earlier than before. And this device works not only in the OR but, perhaps more importantly, also in the less intense and more versatile environment of the clinical laboratory.

This innovation will surely evolve into an autonomous brain pacemaker. Compared with cardiology advances in the 1960s, Dr. Bronte-Stewart adds, "when you talk about a cardiac pacemaker you don't know the settings, you just know it works because *it* does the job." She envisions that "over time the device will self-correct its parameters for specific symptoms because of the work we and others are doing to understand brain signals and which aspect of the disease they are corresponding to."

Soon these parameters may uniquely target movement disorders such as bradykinesia, freezing of gait, and tremor, and eventually other neuropsychiatric diseases such as obsessive-compulsive disorder, intractable depression and possibly Alzheimer's disease. Dr. Bronte-Stewart "can imagine five to ten years from now students and postdocs will say, 'really there was a day when you couldn't read off the brain signals from the pacemaker? That's weird!'" ■