New Neuroimaging Tool Helps Locate Depression Circuit
by James Cavuoto, editor

A team of researchers at Stanford University has developed a new form of neuroimaging to help their quest to uncover the faulty brain circuits involved in depression. The technique, called voltage-sensitive dye imaging, allows intact brain circuits to be viewed in real time, enabling researchers to watch living neurons in action, across entire brain networks.

Writing in the July 6 issue of *Science Express*, the advance online publication of the journal *Science*, Karl Deisseroth, assistant professor of bioengineering and of psychiatry and behavioral sciences, along with Raag Airan, an MD/PhD student in Deisseroth’s lab, described their effort to explain how a range of causes and treatments for depression converge.

They found that in rats the differing mechanisms of depression and its treatment in the end appear to funnel through a single brain circuit. Changes in how the electrical signals spread through the circuit appear to be the cause of depression-related behavior, according to their study.

“I think this will help us make sense of how there can be so many different causes and treatments of depression,” said Deisseroth. “It also helps us understand conceptually how something that seems as hard

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Task Force Addresses Access to New Neurotech Therapies
by James Cavuoto, editor

A newly organized task force representing clinicians, health service providers, payers, and neurotechnology vendors is seeking to expand the availability of neurotechnology devices for individuals with neurological and psychiatric disorders. The National Task Force on Consumer Access to Emerging Neurotechnologies held its inaugural meeting earlier this year and recently published a whitepaper specifically targeted to severe depression. Cyberonics, Inc., the Houston, TX manufacturer of vagus nerve stimulation systems, provided funding for the initial meeting but the group is currently seeking sponsorship from other neurotech device vendors.

The members of the new task force include several clinicians and academics involved with treatment-resistant depression, including Roger Haskett, a professor of psychiatry at University of Pittsburgh, Lawrence Cohen, a professor of pharmacotherapy at Washington State University, and Darin Dougherty from Massachusetts General Hos-
The task force wisely points out the dirty little secret of the neuropharmaceutical industry—that one third of individuals with depression are not successfully treated with currently available medications. This fact needs to be repeated over and over again to all who will listen, if for no other reason than to put into perspective the absurd standards by which neurotech devices are assessed.

It still astounds us that regulatory and reimbursement agencies would balk at a success rate of 40 to 50 percent for a therapy such as VNS or TMS for treatment-resistant depression when pharmaceutical therapies—in aggregate—exhibit at best a 67 percent success rate with the current guideline treatment algorithm. Even with several therapies available to treat Alzheimer's disease, there still is a significant gap between the onset of the disease and when a patient actually starts treatment. This treatment gap is directly tied to the challenges in diagnosing the disease early, before the significant loss of memory, cognition, and activities of daily living. Patients, doctors, caregivers, and the health-care industry are looking for and demanding a solution to this problem.

Over the last nine years, Reid led or directed teams responsible for generating sales revenue of up to $100 million. Reid's bring proven individual and leadership experience in launching eight medical product companies. Three of those products deal directly with the central nervous system and one of those products is currently the most common therapeutic standard treatment for Alzheimer's disease. In his tenure with Pfizer, Reid has won the company's top awards for performance in every position he has held as well as key leadership awards.

Neurotronix Names New CEO to Head Alzheimer's...
Neurotech Business Report

Aspects Medical Receives FDA Clearance for BIS View Monitoring System

Aspects Medical Systems, Inc., the Norwood, MA manufacturer of brain state analysis systems, announced that it has received 510(k) clearance from the U.S. Food and Drug Administration for the BIS View Monitoring system, the company's newest and most advanced brain state monitor. BIS View offers customers a compact design and simplified operation for lower-acuity clinical environments with limited room for monitoring equipment. According to the new indication for use statement cleared by the FDA, BIS monitoring may be used as an aid in monitoring the effects of neuromodulatory agents and may be associated with a reduction in primary anesthetic use and a reduction in emergence and recovery time. Use of BIS monitoring to help guide anesthetic administration may also be associated with the reduction of incidence of awareness with recall in adults during general anesthesia and sedation.

Boston Scientific Announces Precision Plus Spinal Cord Stimulation System

Boston Scientific Corp., the Natick, MA manufacturer of neurostimulation devices, announced the launch of the Precision Plus Spinal Cord Stimulation system, a rechargeable neuromodulation device for treatment of chronic pain of the trunk, back, and limbs. Precision Plus provides physicians with EGI Scan, the first SCS lead image that allows for an improved remote control and charger to simplify control of patient therapy. "Since the launch of the Precision system in 2005, we have delivered the technology and support infrastructure needed to gain more than 25 percent share of the pain management market," said Michael O’neuschek, president of Boston Scientific’s Pain Management Business. EGI Scan (Electronically Generated Lead Scan) technology displays the relative position of implanted leads, within seconds and without using fluoroscopy or x-ray. The information can be used to increase programming efficiencies which can lead to improvements in patient outcomes and treatment office operating efficiencies. The Precision Plus remote control and charger are completely cordless, eliminating the need for cumbersome cords and antennas. The remote control offers the industry's longest wireless range, enabling patients to adjust their pain therapy with simplicity and convenience. The charger is approximately 75 percent smaller and 85 percent lighter than competing chargers, making it convenient and discreet. The charger also features continuous temperature monitoring.

Integra Supports Brain Trauma Foundation’s Guidelines for Severe TBI

Integra LifeSciences Holdings Corp., the Plainsboro, NJ manufacturer of nerve regeneration devices, announced the launch of the Precision Plus Spinal Cord Stimulation system, a rechargeable neuromodulation device for treatment of chronic pain of the trunk, back, and limbs. Precision Plus provides physicians with EGI Scan, the first SCS lead image that allows for an improved remote control and charger to simplify control of patient therapy. "Since the launch of the Precision system in 2005, we have delivered the technology and support infrastructure needed to gain more than 25 percent share of the pain management market," said Michael O’neuschek, president of Boston Scientific’s Pain Management Business. EGI Scan (Electronically Generated Lead Scan) technology displays the relative position of implanted leads, within seconds and without using fluoroscopy or x-ray. The information can be used to increase programming efficiencies which can lead to improvements in patient outcomes and treatment office operating efficiencies. The Precision Plus remote control and charger are completely cordless, eliminating the need for cumbersome cords and antennas. The remote control offers the industry's longest wireless range, enabling patients to adjust their pain therapy with simplicity and convenience. The charger is approximately 75 percent smaller and 85 percent lighter than competing chargers, making it convenient and discreet. The charger also features continuous temperature monitoring.

Integra Supports Brain Trauma Foundation’s Guidelines for Severe TBI

Integra LifeSciences Holdings Corp., the Plainsboro, NJ manufacturer of neurosurgical tools, announced its support for the third edition of the Brain Trauma Foundation’s Guidelines for the Management of Severe Traumatic Brain Injury. The Guidelines are nationally recognized and referenced by many of the leading trauma centers in treatment of patients with traumatic brain injury. The Guidelines were developed by the BTF in association with the American Association of Neurological Surgeons, the Congress of Neurological Surgeons, and the AANS/ CNS Joint Section on Neurotrauma and Critical Care, and incorporate the latest published research findings relevant to the diagnosis and treatment of severe traumatic brain injury. “We are very grateful for Integra’s support of this publication,” said Michael O’neuschek, president of Boston Scientific’s Pain Management Business. EGI Scan (Electronically Generated Lead Scan) technology displays the relative position of implanted leads, within seconds and without using fluoroscopy or x-ray. The information can be used to increase programming efficiencies which can lead to improvements in patient outcomes and treatment office operating efficiencies. The Precision Plus remote control and charger are completely cordless, eliminating the need for cumbersome cords and antennas. The remote control offers the industry's longest wireless range, enabling patients to adjust their pain therapy with simplicity and convenience. The charger is approximately 75 percent smaller and 85 percent lighter than competing chargers, making it convenient and discreet. The charger also features continuous temperature monitoring.

Research Highlights

FDA Approves New Pulse Generators from Cyberonics Inc.

Cyberonics, Inc., the Houston, TX manufacturer of vagus nerve stimulusation systems, announced that the DevicePlusT and DevicePlus Duo-T systems for use in the company’s VNS therapy were approved by the U.S. Food and Drug Administration for commercial release. The DevicePlus generators are 43 percent smaller in volume than the Model 102-generators and incorporate greater functionality, including continuous projection of time to end of service, improved diagnostics, such as direct lead impedance measurement, and faster communication with a programming system.

Feinstein Researchers Identify Two Distinct Parkinson’s Networks

Parkinson’s disease, which causes tremors, rigidity, and slow movements in a million Americans, also targets another brain network that regulates cognitive thought and the ability to carry out everyday tasks. David Edison, head of the Center for Cognitive and Developmental Neuroscience at the Feinstein Institute for Medical Research and his colleagues measured and quantified this network of brain regions during a five-year study of newly diagnosed Parkinson’s patients who agreed to be followed several times over the course of the study. The new report appears in an online version in the journal Brain, the flagship publication of the American Neurological Association that regulates movement and the other cognition—in individuals, and Edison said that it could be used to assess the degenerative disease process and the person’s response to treatments. The study also shows that standard drugs used to treat Parkinson’s alter the areas involved in movement but not those that regulate cognition. The network that grows abnormal over time includes pre-frontal cortex, the same region that is hard-hit in mild cognitive impairment. But Edison said that the system is in pre-clinical disease is different. Thinking that medicines used for Alzheimer’s might help normalize this network, they gave Parkinson’s patients eight weeks of treatment. It didn’t work. In 1999, the researchers recruited 15 patients with early stage Parkinson’s and signed them on to get brain scans at different points over the course of 5 years. Neuroimaging was performed, and the networks to be identified were no surprise: The basal ganglia, thalamus, and brain stem that regulate movement. The scans they used identified areas in this motor network that showed decreased metabolic activity and some areas that had increased metabolic activity. Over time, the cognitive network became apparent. And as the disease progressed and symptoms worsened, this network also took in toll. They are now testing other treatments, including deep brain stimulation, to see if it can impact on the cognitive network.

German Researchers Uncover Mechanism of Pain Distraction

German researchers have pinpointed the brain region responsible for pain’s ability to affect cognitive processing. They have found that this pain-related brain region is distinct from the one involved in cognitive processing interference due to a distracting memory task. Ulrike Bangel and colleagues at the University Medical Center Hamburg-Eppendorf published their discovery in the July 5, 2007 issue of the journal Neuron. To search for the region responsible for pain’s ability to usurp attention, the researchers asked volunteers to perform a cognitive task involving distinguishing images, as well as a working memory task involving remembering images. The researchers asked the volunteers to perform the tasks as they experienced different levels of pain caused by the tapping of their hands by a harmless laser beam. During these tests, the volunteers’ brains were scanned using functional magnetic resonance imaging. The experiments identified the lateral occipital cortex as the cognitive-related area affected by both “working memory load” and pain. This finding was expected, since the LOC is known to be involved in processing images. The researchers next sought to identify the brain region by which pain affects attention. With the volunteers subjected to a varying range of pain levels, the researchers found that the LOC was diminished in the “depressed” rats, a crucial finding that would not be apparent with other experimental methods, Denisenko said. They needed to be able to image a whole circuit simultaneously—and very rapidly—to see the effect. “What surprised me most was how specifically the measure tracked this of circuit-related behavior,” said Arian. “We usually think of psychiatric disorders as fuzzy and intractable, and this study showed me that, with the right tools, we could really put psychiatry on a quantitative framework.”

Toward a Better Understanding of Depression

A research team at the University of Toronto has discovered that different antidepressant drugs affect different brain circuits identified by a new technology that allows researchers to observe how different stimuli affect brain function. In the study, the researchers introduced into the animal brain tissue. As dyed circuits light up and darken in response to electrical activity, very fast high-resolution cameras capture the action. The researchers can observe how different stimuli received by the animal, such as a dose of an antidepressant drug, affect circuit operation.

The researchers used slices of rat brain, Deisseroth said, “like a computer repair technician would take out a circuit board” to test its functional properties. The brain slices, which remain active for many hours, came from parts of the hippocampus, a region that is closely related to memory and learning and that regulates movement. The scans they used identified areas in this motor network that showed decreased metabolic activity and some areas that had increased metabolic activity. Over time, the cognitive network became apparent. And as the disease progressed and symptoms worsened, this network also took in toll. They are now testing other treatments, including deep brain stimulation, to see if it can impact on the cognitive network.
Afferent Corp. Targets Sensory Signals as Novel Neurorehabilitation Strategy
by David Pope, editorial director

Afferent Corp. of Providence, RI, is pioneering a new class of neurostimulation devices that target afferent, or sensory, signals from the peripheral nervous system. Unlike electrodes, the company’s devices use electrical stimulation to activate the efferent neural pathways of the central nervous system, Afferent’s stimulates brainstem and spinal cord to sense signals from the body’s previous institutional investors also participated.

Several pilot clinical studies at the Spaulding Rehabilitation Center and Beth Israel Deaconess Medical Center both Harvard affiliated provided evidence that imperceptible electrical stimulation improves balance and tactile sensitivity in elderly individuals. Other pilot studies showed that applying mechanical vibrations to the soles of the feet improved sway balance in the elderly and in stroke and diabetic patients. Animal studies are continuing at Brown University and the Canadian Centre for Behavioural Neuroscience at the University of Lethbridge, Alberta.

Afferent’s post-stroke rehabilitation clinical studies are underway at Northwestern University’s Feinberg School of Medicine and at the Rehabilitation Institute of Chicago, and Afferent is negotiating additional post-stroke rehabilitation trials at other leading centers.

Harry moved to the position of executive vice president and chief technology officer. James Niemi, who previously worked with Harry at NMT Medical, is now VP of research, and Scott Kellogg is VP of product development. The company has eight employees, and plans to add staff as the products under development approach commercialization.

Although Afferent is initially concentrating on developing insoles for diabetic, and elderly balance markets, the company sees its technology as a new class of device for treating a variety of chronic neurological dysfunctions. In addition to the immediate benefit of improving the sensitivity of mechanoreceptors, the company is pursuing the possibility that subthreshold sensory signals have the potential to induce changes in neural pathways and restore function in the brain through the use of novel technologies for deep brain stimulation.

Several clinical specialists used their experience with neurological disorders as a platform for evaluating new technologies. One of the critical factors in successful recovery of function after stroke or brain injury is the flow of appropriate sensory information from the peripheral limbs. Increasing the sensitivity of the sensory pathways with either electrical or mechanical stimulation could improve standard rehabilitation efforts. If current animal and human studies show positive results, Afferent plans to initiate a pivotal study to determine the benefits in stroke rehabilitation of combining sensory stimulation with physical therapy.

Mechanical and electrical stimulation devices are both under development. A device that combines mechanical and electrical stimulation is being investigated. In such a device, a matraide on the skin generate surface mechanical stimulation in addition to the electronic stimulation of sensory pathways in the brain.

According to Hable, the Stryker investment is an important validation of Afferent’s technology. “They see the neuro area as a promising area of growth and they want to participate in the way for Afferent’s Series B round, which is expected to raise $15 million for product development and clinical trials that could pay off after FDA approval of Afferent’s first product.
Barrow Neurological Institute Performs Leading-Edge Research in Clinical Setting

by James Cavuoto, editor

Barrow Neurological Institute of St. Joseph’s Hospital and Medical Center in Phoenix, AZ is internationally recognized as a leader in neurological research and patient care. Established in 1962, Barrow treats patients with a wide range of conditions, including brain and spinal tumors, cerebrovascular conditions, and neuromuscular disorders.

In addition to its clinical specialties, Barrow features several research laboratories. The Atkinson Pain Research Laboratory, led by Bud Craig, studies connections from the spinal cord to the brain that are involved in bodily “feelings.” The main connection originates in a spinal region called lamina I. Quantitative analyses of lamina I spinothalamic neurons indicate that they serve as “labeled lines” that generate feelings of sharp pain, burning pain, warm, cool, itch, muscle ache, sensual touch, and other sensations related to the body’s physiological condition.

Anatomic work in the laboratory shows that lamina I neurons project their axons first to autonomic spinal and homeostatic brainstem regions, then to a specific thalamocortical relay nucleus called VMpo, which is found only in primates and is greatly enlarged in humans. Craig’s work also shows that stimulation of the vagus nerve causes activity within the same pathway. This finding supports the idea that pain is a reflection of the homeostatic processes in the brain that evolve to maintain the body’s health.

Current work in the laboratory addresses the integration of pain, temperature, itch, and visceral representations within the insular cortex of the primate; the role of the medial thalamus and anterior cingulate cortex in the inhibition of pain by cooling; the association of deep dorsal horn cells with sensorimotor integration (considered for more than 30 years to be pain cells by others); the role of lamina I spinothalamic neurons in injury-induced sensitization (hyperalgesia); and the characterization of lamina I spinobulbar neurons involved in brainstem homeostatic mechanisms.

The Neural Physiology Laboratory, led by Jie Wu, studies the function and pharmacology of recombinant nicotinic acetylcholine receptors transfected into a cloned cell line and natively expressed nAChRs in neurons of the central nervous system using patch-clamp whole-cell and single-channel recordings. Wu’s lab also looks at cellular and molecular mechanisms of epileptogenesis in different epilepsy animal models and epilepsy patient brain tissues, using electrophysiological techniques combined with cellular and molecular biological methods.

The Laboratory of Visual Neuroscience, headed up by Susana Martinez-Conde, investigates the aspects of the neural code that relate to visual perception. One of the ways the lab addresses this is by correlating the eye movements that occur during visual fixation with the spike trains they evoke in single neurons. Since visual images fade when eye movements are absent, it makes sense that the patterns of neural firing that correlate best with fixational eye movements are important to conveying the visibility of a stimulus. The lab has found that bursts of spikes are better related to fixational eye movements than single spikes alone. This suggests that bursts of spikes are more reliable signals than are single spikes.

Calendar

Aug. 23-26 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Lyon France. Contact IEEE EMBS, embc07.ulster.ac.uk
Sep. 15-20 2007 Congress of Neurological Surgeons Annual Meeting, San Diego, CA, contact CNS, neurosurgeon.org
Nov. 3-7 Neuroscience 2007, San Diego, CA. Contact Society for Neuroscience, snf.org.

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