Fall 2005

Stanford Neurosciences Update

For Friends of Stanford University Medical Center

From the Institute Director

Our brain defines us — it makes us think, feel, and gives us our sense of who we are. The members of the Neuroscience Institute at Stanford (NIS) are dedicated to comprehending the potential of neuroscience — unlocking the secrets of the brain.

Many features of brain function are yet to be revealed: how cells become neurons; how neurons interact and form circuits; how circuits learn, remember, and carry out behaviors; and how injury or disease interrupts function.

Realizing the potential of neuroscience requires a culture in which research and clinical care are fully integrated. The NIS is structured to devise new methods of scientific inquiry and to translate discoveries into novel therapies and preventive strategies. It embraces the importance of bringing together scientists, engineers, and physicians, building a new model in which fundamental discoveries can be translated into effective new ways to care for those with neurological and psychiatric disorders.

Targeted working groups will delve into understanding different aspects of the nervous system, including revealing the mechanisms of learning and memory, understanding the processes that lead to neurodegeneration, developing techniques for early diagnosis of diseases such as Alzheimer's or Parkinson's, assessing neural stem cells' potential for treatment of disease, and applying regenerative mechanisms of the nervous system to devise restorative therapies.

To help us in these endeavors, I am pleased to announce the appointment of Karoly Nikolich, PhD, as executive director of the NIS. Dr. Nikolich brings a wealth of experience from his background in biotechnology and science as well as business. I look forward to his unique outlook and bountiful ideas that will undoubtedly aid the NIS in its expansion.

I hope you will be inspired by the work currently being done by Stanford neuroscientists and consider supporting the NIS. Your contribution would be greatly appreciated.

William C. Mobley, MD, PhD
Chair, Department of Neurology and Neurological Sciences
John E. Cahill Family Professor

Stroke

Center Offers Breakthrough Care

The window of opportunity after a stroke is small — treatment is most effective within three hours of the onset of signs and symptoms. But for patients admitted to the Stanford Stroke Center, that window is full of ever-expanding possibilities.

Factor 7, a blood-clotting drug, is proving to be an effective treatment for hemorrhagic strokes.

A year ago, the Center was designated a primary stroke center by the Joint Commission on Accreditation of Healthcare Organizations. This designation means the Center can provide emergency brain imaging and treat patients 24 hours a day with clot-busting medications such as tissue plasminogen activator (tPA). Emergency medical services divert potential stroke patients to certified stroke centers instead of sending them to nearby hospitals. Stanford is the second academic hospital in the

(continued on page 2)

Institutes Team up to Treat Parkinson's Disease

The Neuroscience Institute at Stanford (NIS) and the national Parkinson's Institute will collaborate on projects aimed at accelerating the identification of the biological basis for Parkinson's disease and at developing effective treatments for the disorder.

The collaboration will focus on defining the current state of research in respect to Parkinson's, pointing to gaps in knowledge that limit progress in treatment, applying resources to fill those gaps, accelerating the development of tools and concepts to treat the disorder, and translating these advances to patient care.

"Between our two Institutes, we have a significant number of the top researchers and clinicians in the Parkinson's field," says William Mobley, MD, PhD, the Cahill Family Professor, and director of the NIS. ■

Movement Disorders

Improved Procedure Pinpoints Areas in the Brain

An innovative surgical technique called deep brain stimulation (DBS) can greatly relieve the rigidity and tremors of movement disorders by electrically stimulating an area of the brain. Better still, the procedure used to precisely locate the brain's problem area can now make use of an apparatus that allows for a more comfortable, less time-consuming, and possibly more accurate procedure than in the past.

In deep brain stimulation, surgeons use special markers plus a CT scan and MRI to reference the area for treatment.

Jaimie Henderson, MD, an assistant professor of neurosurgery, helped develop a replacement for the stereotactic frame previously used with patients. Originally designed to help surgeons perform craniotomies, the frameless stereotactic approach is now being used for functional neurosurgeries such as DBS, where surgeons treat brain anatomy that appears normal but contains malfunctioning circuits — as in Parkinson's disease, chronic pain, or epilepsy.

The new approach provides many benefits for Parkinson's patients. "During the procedure, you want the firing patterns in the brain to be as abnormal as possible to accurately locate the target," says Dr. Henderson. To achieve this, patients must be off medications, which means their symptoms of stiffness, immobility, and shaking worsen.

A radiologist performs an MRI with intravenous contrast dyes before surgery to identify the target and helps locate blood vessels, which the surgeon must skirt to prevent bleeding.

"The day before surgery a surgeon numbs five spots on the scalp with local anesthetic, makes small incisions, and screws small titanium markers into the skull," says Dr. Henderson. Next, a CT scan is taken to compensate for any distortions on the MRI. All images are fused into a three-dimensional composite. Next, the surgeon targets and defines the entry point to avoid surface blood vessels. With the previous system, these images had to be taken with the stereotactic frame in place, increasing the complexity and length of the procedure.

Because the system can automatically adjust for slight head movements, patients need not remain entirely immobilized.

On the day of surgery, two cameras track the position of a reference frame. This creates a stable marker for the location of the patient's head. The markers rigidly affixed the day before correlate with those on the scans, giving the surgeon a kind of X-ray vision and enhancing accuracy. Because the system can automatically adjust for slight head movements, patients need not remain entirely immobilized.

Next, the surgeon refines the target area and inserts a stimulating electrode, which is connected by wires to a pacemaker-like device implanted beneath the patient's collarbone. "It is activated about a month later but can take several months of programming to get the desired result," says Dr. Henderson.

Dr. Henderson hopes to improve patient comfort even more by using X-rays to automatically achieve registration, thereby avoiding the need for markers. ■

Stroke Center

(continued from page 1)

country to be stroke certified.

The Stanford Stroke Center provides the highest level of multidisciplinary acute stroke care, staffed by a team of neurologists, neurosurgeons, and radiologists. Center staff use a code system that takes greatest advantage of stroke's narrow window of opportunity. Paramedics notify the ER of patients' imminent arrival, which allows physicians to quickly administer treatments, greatly enhancing their results.

Experts in the Stroke Center are involved in cutting-edge research, developing new protocols and tools to improve the diagnoses, treatment, and prevention of stroke.

For example, Christine Wijman, MD, an assistant professor of neurology and neurological sciences and director of the Stanford Neurocritical Care program, is working on a multicenter study of Factor 7, a blood-clotting drug originally designed to treat bleeding problems in patients with hemophilia. The results of an earlier trial in hemorrhagic stroke — in which a blood vessel ruptures, spilling blood into the brain — were extremely encouraging, she says.

"Patients were more likely to have a smaller hemorrhage, showed a lower mortality rate, and were less severely handicapped if they received the drug," says Dr. Wijman, Stanford's principle investigator on this study. If results are confirmed in the Phase III trial, Factor 7 could become the standard treatment for hemorrhagic stroke, just as tPA is for ischemic stroke, which is caused by blocked blood vessels.

Another area of research for Dr. Wijman involves lowering patients' temperatures to 4 degrees below normal for 24 hours to protect the brain after ischemic stroke.

"When the body and brain are cooled, the brain requires less oxygen," she says. "We think that cooling the brain slows or blocks a number of cascades that lead to further brain injury after an ischemic stroke."

The first patient to benefit from this treatment at Stanford had received tPA but still had substantial weakness on the right side several hours after treatment. Following 24 hours of cooling, he improved dramatically. "Ten days after his stroke, he walked out of the hospital and is at home now, where he can shower and dress on his own," Dr. Wijman says. ■