Demystifying the Brain

Through pioneering research and clinical care, BWH scientists and physicians are unraveling the brain’s inner workings and developing promising treatments for disease.
EVEN TO TRAINED EYES, THE SUBTLE DIFFERENCES BETWEEN A SCHIZOPHRENIC BRAIN AND A NORMAL ONE CAN BE DIFFICULT TO DISTINGUISH. UNTIL RECENTLY, THE TOOLS USED TO EVALUATE PATIENTS WHO MIGHT HAVE THE DISEASE WERE RELATIVELY CRUDE, MAKING IT CHALLENGING TO SPOT THE SMALL, BUT SIGNIFICANT, STRUCTURAL ANOMALIES CONSIDERED HALLMARKS OF THE DISEASE.

But thanks to technological improvements, many of which can be credited to two Brigham and Women’s scientists—Martha Shenton, PhD, director of the Psychiatry Neuroimaging Laboratory, and Ron Kikinis, MD, director of the Surgical Planning Laboratory—schizophrenia research has progressed rapidly over the past decade. Advancements in magnetic resonance imaging, or MRI, and new image-processing tools that extract information from MR scans allow physician-scientists to explore the brain in vivo. For example, they have been able to confirm the long-held theory that schizophrenia is a brain disorder.

Even so, a definitive test for schizophrenia remains elusive. Clinicians rely on conversations with patients about their symptoms to diagnose it, a method that is entirely too subjective.

“The goal for schizophrenia researchers,” says Kikinis, “has been—and still is—to develop a tool to quantify the diagnosis and take the subjectivity out of it.”

A disabling mental condition characterized by psychosis, schizophrenia afflicts about 1 percent of the population. Sufferers tend to withdraw from people and activities in the world around them and retreat into a universe of delusions or a separate reality.

“It’s terribly tragic,” says Shenton. “Schizophrenia sometimes seems to come out of nowhere. It generally strikes in early adulthood, at the threshold of what should be the most productive period of life. The cost to the family and society is huge.”

A TECHNOLOGICAL REVOLUTION

MRI was the first device that could measure the soft-tissue differences in the brains of people with schizophrenia and those without the disorder. It uses high-field-strength magnets and radio frequencies to produce detailed images.

Although CT scans predated MRI and can show brain structures and cerebrospinal fluid, they cannot distinguish between white and gray matter, the soft tissues in which most of the anatomical changes associated with schizophrenia have been identified.

Shenton started working at BWH in 1987, and the following year, she teamed up with Kikinis to improve MRI and the tools that extract information from the pictures it generates. Applying image-processing tools originally developed for satellite image analysis to MR scans from schizophrenia patients, they have been able to construct 3-D images of the brain and zero in on certain areas. They have focused on gray matter, the brain’s outer “bark,” as well as white matter, the brain’s inner core. Fiber tracts that connect various areas of the brain with each other and with the rest of the nervous system make up the white matter.
“We can segment the brain into gray matter, white matter and cerebrospinal fluid,” says Shenton. “We can also look at smaller regions of the brain to determine what role they may play in schizophrenia.”

A new generation of MR techniques makes it possible to quantify further the volume of the whole brain, as well as small brain structures, providing researchers and clinicians with even more detailed assessments of the brain anomalies associated with schizophrenia and other neurological disorders.

Among these newer techniques: diffusion tensor imaging, or DTI, and functional MRI. DTI analyzes the movement of water molecules in and around the fibers that connect different parts of the brain. These scans help researchers better understand the functional and anatomical differences in schizophrenia sufferers’ neural pathways, the routes messages take as they zip from one area of the brain to another.

Functional MRI measures blood flow in the brain while an individual performs such critical functions as thinking, speaking or moving. Investigators believe that functional changes in the brains of schizophrenics are related to structural changes in other brain regions. Clinicians are fusi-

Magnetic resonance imaging brains scans from a healthy patient (left) and one diagnosed with schizophrenia (right). Note the increase in cerebrospinal fluid (dark areas) in the schizophrenic brain. Increases in cerebrospinal fluid cause decreases in white and gray matter volume, a hallmark of schizophrenia.

Kikinis recently started the third year of a five-year, $19.2-million grant from the National Institutes for Health to create the National Alliance for Medical Imaging Computing, or NA-MIC. Led by BWH, this multi-institutional consortium strives to improve the software that analyzes MR, CT and other images from patients with any number of conditions. Researchers from Shenton’s Psychiatry Neuroimaging Laboratory, Kikinis’ Surgical Planning Laboratory, the BWH Center for Bioinformatics, MIT, the University of North Carolina and the University of Utah are involved in schizophrenia research under the NA-MIC umbrella.

Their goal now is to link the characteristic structural and functional abnormalities seen in schizophrenia with the neural circuits that relate to inattention, delusions and hallucinations. They also want to determine whether the abnormalities are static or worsen over time.

“We now have the tools to view and understand the brain, which is incredibly exciting,” says Shenton. “Our increased knowledge will likely lead to earlier intervention and new treatments. Perhaps it will even help us prevent this devastating disorder.”