# Can Brain Scans See Depression?

By BENEDICT CAREY

They seem almost alive: snapshots of the living human brain.

Not long ago, scientists predicted that these images, produced by sophisticated brain-scanning techniques, would help cut through the mystery of mental illness, revealing clear brain abnormalities and allowing doctors to better diagnose and treat a wide variety of disorders. And nearly every week, it seems, imaging researchers announce another finding, a potential key to understanding depression, attention deficit disorder, anxiety.

Yet for a variety of reasons, the hopes and claims for brain imaging in psychiatry have far outpaced the science, experts say.

After almost 30 years, researchers have not developed any standardized tool for diagnosing or treating psychiatric disorders based on imaging studies.

Several promising lines of research are under way. But imaging technology has not lived up to the hopes invested in it in the 1990's - labeled the "Decade of the Brain" by the American Psychiatric Association - when many scientists believed that brain scans would turn on the lights in what had been a locked black box.

Now, with imaging studies being published at a rate of more than 500 a year, and commercial imaging clinics opening in some parts of the country, some experts say that the technology has been oversold as a psychiatric tool. Other researchers remain optimistic, but they wonder what the data add up to, and whether it is time for the field to rethink its approach and its expectations.

"I have been waiting for my work in the lab to affect my job on the weekend, when I practice as a child psychiatrist," said Dr. Jay Giedd, chief of brain imaging in the child psychiatry branch at the National Institute of Mental Health, who has done M.R.I. scans in children Monday through Friday for 14 years. "It hasn't happened. In this field, every year you hear, 'Oh, it's more complicated than we thought.' Well, you hear that for 10 years, and you start to see a pattern."

Psychiatrists still consider imaging technologies like M.R.I., for magnetic resonance imaging, and PET, for positron emission topography, to be crucial research tools. And the scanning technologies are invaluable as a way to detect physical problems like head trauma, seizure activity or tumors. Moreover, the experts point out, progress in psychiatry is by its nature painstakingly slow, and decades of groundwork typically precede any real advances.

But there is a growing sense that brain scan research is still years away from providing psychiatry with anything like the kind of clear tests for mental illness that were hoped for.

"I think that, with some notable exceptions, the community of scientists was excessively optimistic about how quickly imaging would have an impact on psychiatry," said Dr. Steven Hyman, a professor of neurobiology at Harvard and the former director of the National Institute of Mental Health. "In their enthusiasm, people forgot that the human brain is the most complex object in the history of human inquiry, and it's not at all easy to see what's going wrong."

For one thing, brains are as variable as personalities.

In a range of studies, researchers have found that people with schizophrenia suffer a progressive loss of their brain cells: a 20-year-old who develops the disorder, for example, might lose 5 percent to 10 percent of overall brain volume over the next decade, studies suggest.

Ten percent is a lot, and losses of volume in the frontal lobes are associated with measurable impairment in schizophrenia, psychiatrists have found. But brain volume varies by at least 10 percent from person to person, so volume scans of patients by themselves cannot tell who is sick, the experts say.

Studies using brain scans to measure levels of brain activity often suffer from the same problem: what looks like a "hot spot" of activity change in one person's brain may be a normal change in someone else's.

"The differences observed are not in and of themselves outside the range of variation seen in the normal population," said Dr. Jeffrey Lieberman, chairman of the psychiatry department at Columbia University Medical Center and director of the New York State Psychiatric Institute.

To make matters even more complicated, many findings are disputed. In people with severe depression, for instance, researchers have found apparent shrinkage of a part of the temporal lobe called the hippocampus, which is critical for memory. But other investigators have not been able to replicate this finding, and people with injuries to the hippocampus typically suffer amnesia, not depression, psychiatrists say.

For problems like attention-deficit disorder and bipolar disorder, the experts say, psychiatrists have much less research on which to base their theories.

Most fundamentally, imaging research has not answered the underlying question that the technology itself has raised: which comes first, the disease or the apparent difference in brain structure or function that is being observed?

For a definitive answer, researchers would need to follow thousands of people from childhood through adulthood, taking brain scans regularly, and matching them with scans from peers who did not develop a disorder, experts say. Given the expense and difficulty, such a study may never be done, Dr. Hyman said.

One investigator has used imaging research to fashion a small, experimental psychiatric treatment.

In a series of studies of people with severe depression, Dr. Helen Mayberg, a professor of psychiatry at Emory University in Atlanta, found a baffling pattern of activity.

Using PET scanning technology, Dr. Mayberg found sharp dips and spikes of activity in about a half-dozen areas of these patients' brains as their moods improved while they were taking either antidepressant drugs or placebos.

The changes were similar in all patients, but it was difficult to tell how the scattering of the dips and spikes were related.

By analyzing the peaks and valleys on the scans as part of a circuit - networked together, like a string of Christmas lights - Dr. Mayberg found that one spot in particular seemed to modulate the entire system, like a transformer or a dimmer.

She confirmed the importance of this spot, called Brodmann area 25, by scanning the brains of mentally healthy people while they remembered painful episodes from their lives: while sad they, too, showed increased activity in this area.

In March, Dr. Mayberg and a team based at the Rotman Research Institute in Toronto reported on six patients who had had electrodes implanted in their brains next to Brodmann area 25.

All had been severely depressed for at least a year, and they had responded poorly to available therapies. The implanted electrodes, often used to treat Parkinson's disease, produce a current that slows neural activity, for reasons scientists do not yet understand.

So far, the researchers reported in the journal Neuron, four of the six people have shown significant and lasting recovery; all four are still on antidepressant drugs but at reduced doses. And all four have returned to work or their usual routines, Dr. Mayberg said.

The widely reported experiment has generated more than 300 requests from people to be considered for the operation, she added.

"It's very important to understand that this is experimental, and the next step is to replicate what we did, with a placebo, and that could send us right back to the drawing board," Dr. Mayberg said in an interview.

The findings so far are encouraging, she said, "but the idea that this is something for every severely depressed patient - well, shame on us if we suggest that. The brain is a very big place and we had better have a very good idea of what we're doing before holding this out as a treatment."

Many people would rather not wait for the science of imaging to mature, however. At clinics in California, Washington, Illinois, Texas and elsewhere, doctors offer brain scans to people with a variety of conditions, from attention-deficit hyperactivity disorder, often called A.D.H.D., to depression and aggressive behavior.

Dr. Daniel Amen, an adult and child psychiatrist based in Newport Beach, Calif., said he performed 28,000 scans on adults and children over the past 14 years, using a technique called Spect, or single photon emission computed tomography.

In an interview, Dr. Amen said that it was unconscionable that the profession of psychiatry was not making more use of brain scans. "Here we are, giving five or six different medications to children without even looking at the organ we're changing," he said.

He said the scans had helped him to distinguish between children with attention deficit problems who respond well to stimulants like Ritalin and those who do poorly on the drugs. In a series of books and medical articles, Dr. Amen argued that the images helped convince people that the behavior problems had a biological basis and needed treatment, with drugs or other therapies.

"They increase compliance with treatment and decrease the shame and guilt" associated with the disorders, he said.

At the Brainwaves Neuroimaging Clinic in Houston, doctors use the scans to diagnose and choose treatment for a range of psychiatric problems, according to a clinic spokeswoman. And a variety of doctors advertise the imaging services, particularly for attention-deficit disorder, on the Internet. But the experts who study imaging and psychiatry say there is no evidence that a brain scan, which can cost more than $1,000, adds significantly to standard individual psychiatric exams.

"The thing for people to understand is that right now, the only thing imaging can tell you is whether you have a brain tumor," or some other neurological damage, said Paul Root Wolpe, a professor of psychiatry and sociology at the University of Pennsylvania's Center for Bioethics.

He added, "This imaging technology is so far from prime time that to spend thousands of dollars on it doesn't make any sense."

The big payoff from imaging technology, some experts say, may come as researchers combine the scans with other techniques, like genetic or biochemical tests. By radioactively marking specific receptors in the brain, for example, researchers are using brain scans to measure how brain chemicals known to affect mood, like dopamine, behave in people with schizophrenia, compared with mentally healthy peers.

Imaging researchers are also studying depression-related circuits to see how they may arise from genetic variations known to put people at risk for depression.

And as always, the technology itself is improving: a new generation of M.R.I. scanners, with double the resolution power of the current machines, is becoming more widely available, Dr. Lieberman said.

"With increased resolution, we'll be able to do more sensitive and more precise work, and I would not be surprised if anatomy alone based on volume will be a diagnostic feature," he said. "We have gained an enormous amount knowledge from thousands of imaging studies, we are on the threshold of applying that knowledge, and now it's a matter of getting over the threshold."

But for now, neither he nor anyone else can say when that will happen.