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A CONVERSATION WITH NANCY C. ANDREASEN

Using Imaging to Look at Changes in the Brain

By CLAUDIA DREIFUS

Dr. Nancy C. Andreasen concentrates on the big questions. A neuroscientist and psychiatrist at the University of Iowa, she uses M.R.I. to ask questions like: How do the nervous systems of extremely creative people differ from those of the rest of us? How is the brain physiology of the mentally ill different from that of normal people? For nearly two decades, she has been conducting a study that tracks long-term changes in the brain. We spoke this summer when she visited New York City. An edited version of a three-hour conversation follows:

Q. HOW DID YOU BECOME A PSYCHIATRIST?

A. I was an English professor in the early 1960s. I'd done a book on John Donne. Then, in 1964, I gave birth to my first child and nearly died from a postpartum infection — the very thing that had killed millions of birthing women in the centuries before antibiotics. As I recovered, I realized I had been given back my life, and that caused me to rethink everything in it. I decided to quit literature studies and go back to school to become a doctor.

From the outset, I knew I wanted to do research and patient care. Because I relish complexity, I chose psychiatry — it's more complicated than neurology. And I chose brain research because the brain is the most complicated organ in the body. I wanted to do something as important as the discovery of penicillin, the thing that had saved me.

Q. YOU PIONEERED THE USE OF IMAGING TECHNOLOGY FOR LEARNING ABOUT THE PHYSIOLOGY OF THE BRAIN. HOW DID THE IDEA OF USING CAT SCANS AND M.R.I.'S AS A RESEARCH TOOL COME TO YOU?

A. My first patient was a schizophrenic. After working with him, I wanted to understand how this terrible disease developed, how to stop it and to find better treatments. Right away, I began searching for new tests to assay brain activities. With the technology we had at that time, you couldn't see brain differences easily. A lot of our information came from autopsies done on patients, but that was of limited use because you had nothing to compare it to.

But then, in the early 1970s, CT scans came along. They got pictures of the inside of a living patient's brain. I recognized the potential immediately. The problem was convincing my colleagues. CT scans involved exposing patients to radiation. When I went to the human experimentation committee at my medical school, they went, "We don't want you subjecting patients to radiation. Besides, you're not going to find anything that way, anyway." It took a long time to convince them.

Q. TODAY, IMAGING STUDIES ARE ONE OF THE MAINSTAYS OF NEUROSCIENCE. WHEN DID ATTITUDES CHANGE?

A. In the early 1980s, when magnetic resonance imaging came on line. M.R.I.'s did not expose patients to radiation, and you could see brain structures in exquisite detail. I decided to use it for a longitudinal study of brain changes over a long period of time. We're asking: Is schizophrenia a neurodegenerative disease like Alzheimer's?

In 1989, I began to collect subjects — some with schizophrenia and some not — and began taking pictures of their brains. With the schizophrenics, we began seeing them at the first onset of their disease, which is usually at around age 24. We recruited about 538 people with schizophrenia. Eighteen years later, we're still following 305.

Q. AND WHAT HAVE YOU FOUND?

A. I haven't published this yet. But I have spoken about it in public lectures. The big finding is that people with schizophrenia are losing brain tissue at a more rapid rate than healthy people of comparable age. Some are losing as much as 1 percent per year. That's an awful lot over an 18-year period. And then we're trying to figure out why. Another thing we've discovered is that the more drugs you've been given, the more brain tissue you lose.

Q. WHY DO YOU THINK THIS IS HAPPENING?

A. Well, what exactly do these drugs do? They block basal ganglia activity. The prefrontal cortex doesn't get the input it needs and is being shut down by drugs. That reduces the psychotic symptoms. It also causes the prefrontal cortex to slowly atrophy.

If I were developing new drugs, I'd switch targets. Till now it's been chemically formulated targets. I believe we should be thinking more anatomically and asking, "With schizophrenics, which brain regions are functioning abnormally?"

Q. ARE YOU WORRIED YOUR FINDINGS MIGHT BE MISUSED?

A. The reason I sat on these findings for a couple of years was that I just wanted to be absolutely sure it was true. My biggest fear is that people who need the drugs will stop taking them.

Q. WHAT ARE THE POLICY IMPLICATIONS OF THIS FINDING?

A. Implication 1: that these drugs have to be used at the lowest possible dose, which often doesn't happen now. There's huge economic pressure to medicate patients very rapidly and to get them out of the hospital right away. Implication 2: we need to find other drugs that work on other systems and parts of the brain. Implication 3: whatever medications we use need to be combined with more nonmedication-oriented treatments, like cognitive or social therapies.

Q. IN YOUR LONGITUDINAL STUDY, ARE YOU ALSO LOOKING AT HOW THE NORMAL BRAIN AGES?

A. Yes. I've been asking, "At what point is human brain maturation complete and at what point do our brains naturally decline and lose tissue?" The answer is: the human brain continues to mature till about 25. At about 25, it plateaus for about 20 years, and at about 45, we start to lose brain tissue.

But it's interesting: we lose brain tissue, but we don't necessarily lose cognitive capacities. A lot of people at 50, 60, 70 or 80 are quite sharp. I can quantify their brain tissue and see they've lost quite a bit from what would be normal for a 45-year-old, but their cognitive abilities are not at all impaired.