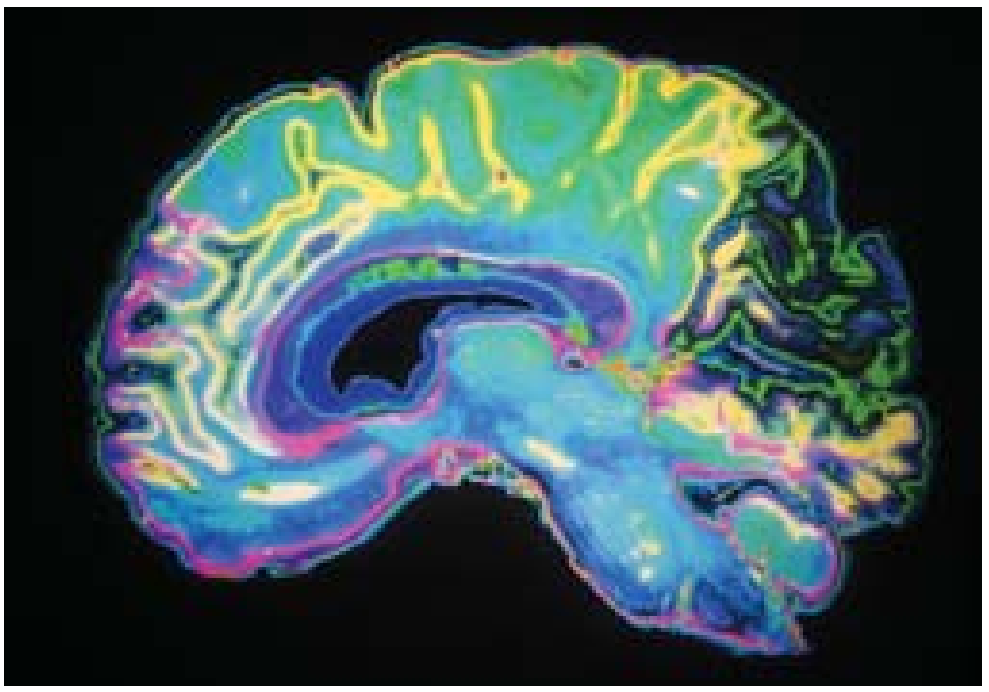
Pioneering schizophrenia research

Dr. Nancy Andreasen is a neuroscientist and psychiatrist at the University of Iowa in the US. An established scholar of English literature, Andreasen radically changed her career after a severe illness and focused her talents on medicine, psychiatry and the subtle disease of schizophrenia. She pioneered the use of imaging technology for psychiatric research, which is now a fundamental tool of neuroscience. For her work, Andreasen has won numerous awards including the US National Medal of Science. _Medical Tribune's Radha Chitale_ spoke with Andreasen recently in Singapore.



Andreasen was one of the first to use CT and MRI scans to study schizophrenia.

Why did you pursue medicine after earning a doctoral degree in English literature and securing a professorship at a university?

My husband and I agreed we would go to the first place that offered us both jobs. We moved to Iowa City, Iowa, US, where he was an orthodontist and I got a job with the English department at the University of Iowa. At that time, women were not particularly welcomed into anything and I was actually the first woman to be hired in the school's English department.

We got to Iowa and I realized I was expecting our first child. I had expected not to miss any teaching time but after delivery I became ill with puerperal sepsis, which is a postpartum infection. I was re-hospitalized, put on antibiotics and realized my life had been saved. If this happened 100 years ago, I would have died.

That led me to evaluate what I wanted to do with my life and my abilities. I thought, if I stay in English, I might inspire a few kids but I'm not going to change them very much. If I were to go into a field like medicine, I might find something that could affect thousands or millions of people the way antibiotics have affected me. So I made the decision to go into medical school and be a research scientist.

What kinds of reactions did you get as a wife and mother attempting to enter a demanding field?

I had very few supporters. When I applied to the University of Iowa's Carver College of Medicine, they initially made the decision to turn me down because I was married and had a child. That was just about the kiss of death. And I had an A-average and very high scores on the medical school admissions tests. But I had a good friend, a pathologist, who lived across the street and knew someone on the admissions committee. He went to him and said "if you don't admit Nancy, you're going to be making a serious mistake."

I had a small number of good friends who were medical students who were supportive. My husband was very supportive and that was a big deal. But the majority of people, including professors, were not.

How did you balance work and family life during that time?

By getting very little sleep. I used to stay up with my daughter Susan, who was 2 years old, until about 8:30 pm, put her to bed and start studying until about midnight. Then I would set the alarm for 4:00 am, get up and study again.

You specialized in neuroscience and psychiatry. What drew you to the field?

I'm a very conceptual person but also a person who's interested in subtle, complicated things. This is what you get when you study the brain. And between neurology and psychiatry, psychiatry is much more complicated and has a greater health burden. We like to say that neurology is a specialty that has 100 diseases and 10 patients while psychiatry is a specialty with 10 diseases and 100 patients. A huge number of people throughout the world suffer from mental illness.

In psychiatry, the illnesses are complicated to diagnose and they can be complicated to treat. And yet for many of the illnesses we have good outcomes. Mood disorders can usually be treated very successfully. I chose to focus on schizophrenia because I was fascinated by how the human brain could produce such bizarre thoughts and experiences. It's a real mystery.

What are the most common misconceptions about people with schizophrenia?

Probably the most common misunderstanding is that schizophrenia is a split personality — it's not. We now understand that schizophrenics have mis-wired circuits in the brain creating missed connections.

Another misunderstanding is that people with schizophrenia are just unconventional, original thinkers. This is a romanticized view of schizophrenia, that madness is a kind of empowering thing. Nobody who knows it well would ever romanticize it. But it is a treatable illness.

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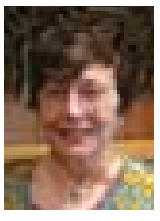
>
> *– Dr. Nancy Andreasen*



How had people been studying brain activity in mentally ill patients before imaging technology?

In a way I wasn't very bright when I chose psychiatry because I didn't realize that there weren't very many ways available to understand the brain. Technologies that were available measured breakdown products of chemicals that we know occur in the brain, but those chemicals are metabolized all over the body. There were procedures like pneumoencephalography and cerebral angiography that were too invasive. What was left was figuring out ways to assess cognition, and I spent quite a bit of time evaluating language patterns and abnormalities in schizophrenia because of my background in English literature. But none of these possibilities was a panacea.

How did you incorporate computed tomography (CT) and magnetic resonance imaging (MRI) technologies into brain research?

I'll always remember the first time I saw a CT scan because here it was — a picture of the brain! When CT became available in the mid-1970s, it was the first non-invasive form of imaging. Unfortunately, it involved a modest amount of radiation exposure and I could not get permission to be the first to use CT to study the brain in mental illnesses. Eventually we got permission and I did a lot of early work with CT scanning.

And then MRI became available and those pictures were thrilling. They looked like slices of postmortem brain tissue, they were that precise. I said this is going to be it — this is a way to do *in vivo* neuroanatomy. But it's not about looking at the picture, it's about finding ways to measure information embedded in the picture. Almost immediately we began to develop software that let us measure various aspects of the brain. We measured the volume of tissue, volume of grey matter, volume of the frontal lobes, and so on. We were completely at the forefront in the use of imaging technology in psychiatry and other brain disorders.

What were some of the initial, important findings that resulted from your research?

The first big thing using CT imaging was that patients with schizophrenia had measurable brain abnormalities, on average. At the time that was a big deal because psychoanalysis was still very prevalent and a lot of people didn't think that schizophrenia was a brain disease.

With MRI, we could look at very specific brain regions and we did the first quantitative study with MRI to provide evidence that schizophrenia was a neurodevelopment disorder. Compared to healthy, normal volunteers, people with schizophrenia had less tissue volume. Proportionally, the volume decreased in the frontal lobes. They also had smaller cranial volume, which meant that something had gone wrong in neurodevelopment.

From there the technology gets more sophisticated, with positron emission tomography (PET) scans and functional MRI imaging, as do the questions we answer. The real wave of the future is integrating imaging with genomics and trying to figure out the interactions between genes and gene products and measuring those with brain imaging.

What new research are you working on?

One of the things we have worked on in the past is to figure out what the long term course of schizophrenia is and how phases of the illness can be defined, what the correlates are, and what kinds of treatments will produce good outcomes. We only developed a scientific definition of remission from schizophrenia in 2005, and once applied, we discovered that about half of people with schizophrenia are in remission for at least 6 months. A fairly large number are in remission for up to 6 years.

Now we are working on having an equally good definition of what constitutes a relapse in schizophrenia using a large pool of MRI, cognition and psychosocial function data from a prospective longitudinal study begun in 1987. This will help us examine the brain changes and correlates associated with relapse, if we can predict who is likely to have a relapse and what types of medications are most likely to prevent it.

We are also starting the first clinical drug trial I've done on long-acting injectables compared to oral treatment to improve how patients take medication. We plan to explore whether these long-acting injectables are more likely to prevent relapses, since the patients who receive them will have a steadier and more reliable treatment program. And then in turn, we will be able to explore whether reducing relapse also reduces the progressive brain changes that occur over time that we have observed in some patients who have schizophrenia. These medications offer the possibility for intervention early in the illness that may effectively prevent later social, cognitive, or brain deterioration. MT