

Brain tissue reveals possible genetic trigger for schizophrenia

March 28 2007

A study led by scientists from the University of North Carolina at Chapel Hill may have identified a molecular mechanism involved in the development of schizophrenia.

In studying the postmortem brain tissue of adults who had been diagnosed with schizophrenia, the researchers found that levels of certain gene-regulating molecules called microRNAs were lower among schizophrenia patients than in persons who were free of psychiatric illness.

"In many genetic diseases, such as Huntington's disease or cystic fibrosis, the basis is a gene mutation that leads to a malformed protein. But with other complex genetic disorders – such as schizophrenia, many cancers, and diabetes – we find not mutated proteins, but correctly formed proteins in incorrect amounts," said study lead author and UNC professor of psychiatry Dr. Diana Perkins.

The research appears this week in the online edition of the journal *Genome Biology*. "To our knowledge this study is the first to associate altered expression of microRNAs with schizophrenia," the authors stated.

Since the 1950s, scientists have known that the genetic code stored in DNA is first transcribed into messenger RNA (mRNA) which is then the template from which the body's protein building blocks are made. MicroRNAs are a newly discovered class of mRNA that does not carry

the code for a protein. Instead, these tiny strands of RNA act by binding to matching pieces of the protein coding mRNA, thus preventing the translation of mRNA to protein. When a cell needs certain proteins, the microRNAs may disconnect, thus allowing protein expression to resume.

Using postmortem prefrontal cortical brain tissue of people with schizophrenia and persons who had no psychiatric illness, the researchers found for the first time a significant difference in the microRNA expression profile. Fifteen microRNAs were expressed at a lower level and one at a higher level in the brain tissue from persons with schizophrenia. The basic activity of this "executive" brain region is the orchestration of thoughts and actions in accordance with internal goals.

Previous studies have shown that microRNAs play a role in regulating brain development. They also figure importantly in "synaptic plasticity," the ability of neurons to make connections with one another. "And those connections between neurons come and go all the time. It's a normal process for them to be pruned and grow again, depending on what the brain needs to do to interact with the environment," Perkins explained.

"There is growing evidence that schizophrenia may related to disordered synaptic plasticity," she added. "Our study found a striking, significant difference in microRNA expression between people with schizophrenia and healthy people. Using bioinformatic analyses, we found that the distinguishing microRNAs appear to regulate genes involved in synaptic plasticity."

Acknowledging this was a pilot study, Perkins and her colleagues plan further research with larger tissue samples.

Source: University of North Carolina School of Medicine

Citation: Brain tissue reveals possible genetic trigger for schizophrenia (2007, March 28)
retrieved 9 April 2024 from
<https://medicalxpress.com/news/2007-03-brain-tissue-reveals-genetic-trigger.html>

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