The Persistence of Mental Illness

By Peter D. Kramer on June 02, 2008 in In Practice

If schizophrenia is simply harmful, if it offers no benefits for survival, how has it persisted over generations? This question is especially puzzling since sufferers have severe problems in social functioning and tend to produce relatively few children.

A partial answer is emerging in new genetics research. A letter just posted in advance of publication in Nature Genetics confirms and expands on some of the findings I reported on recently about random mutations and mental illness. The new research — conducted by Maria Karayiorgou at Columbia University but carried out with Afrikaners in South Africa — looked at people with schizophrenia who come from families with no history of the disease. The patients had a high rate of a particular type of genetic anomaly, copy number (or CN) mutations. Their genes might be normal, but there were too many or too few of them.

In a number of cases, the copy variations were in genes already thought to be linked to schizophrenia. For various other reasons, the researchers believe that the mutations are causal, that they have a major role in producing the severe mental illness.

Some, perhaps most, cases of schizophrenia are familial. But in this population of patients representing “sporadic” cases, most of the CN mutations were not inherited but had arisen “de novo” in the patient with schizophrenia. In other words, any liability to mental illness was not inherited but had occurred in the development of the egg or sperm, or during early maturation. On the other hand, some CN mutations were inherited, suggesting that such abnormalities can be passed on. CN mutations have now been implicated in a number of disorders, including Parkinson’s and Alzheimer’s diseases, autism, and certain cancers.

This mechanism for producing schizophrenia may not be common. But the new finding suggests one reason mental illnesses might remain prevalent even when they confer an evolutionary disadvantage. They can be created anew in each generation, though mutations.

Also, the research helps explain why no one has found a unique gene for schizophrenia. Normal genes can help cause the disease, if they exist in the wrong number. And a few different genes showed the copy number variations, so genetic defects at various sites seem to contribute to schizophrenia. Since some of the mutations are passed on, familial schizophrenia is likely to prove diverse in this way as well.

This new research presents substantial problems for the “myth of mental illness” argument. We can see why scientists have not discovered a single gene for the disease. It has varied causes — and some are in areas that science could not reach until just now. (The link between epigenetics and mental illness may turn out to have similar implications.) At the same time, the genetic basis for schizophrenia is becoming increasingly apparent.
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Like depression, schizophrenia has been subject to romanticization, for example in R. D. Laing's suggestion that the disorder arises in response to "double binds" in dysfunctional families. This formulation is appealing, but it may simply be wrong; if it is, it may have led to misguided forms of psychotherapy. The question is not what we would prefer to believe, but what we must know in order to help people in pain.

Very likely there are environmental contributors to schizophrenia, including social ones. But inheritance may turn out to play a predominant role. In a press interview, Karayiorgou has expressed hope that exploration of the genes implicated in her studies will lead to guidance regarding treatment and prognosis. Before that, the findings may allow for early diagnosis, using markers no one had imagined until recently.