SCHIZOPHRENIA

Is it hereditary, is it environmental or is it a combination of both factors?

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by Robert J. Trotter

The nature-nurture controversy has been brought to bear on almost every facet of the human condition. Alcoholism, criminality, homosexuality, I.Q. and an array of psychoses and neuroses have all been ascribed, at one time or another, to either genetic or environmental factors. But arguments on both sides have been attacked as inconclusive and, like the chicken and the egg, no one has yet proved which came first. In the case of schizophrenia, however, the genetic hypothesis may be losing ground or at least heading for a compromise.

The idea that schizophrenia could be genetically caused took hold as statistics made it obvious that the disease ran in families. David Rosenthal of the National Institute of Mental Health explained the thinking behind this theory at a recent meeting of the National Academy of Sciences. "With a few rare exceptions," he said, "the incidence of schizophrenia in first-degree relatives of schizophrenic probands [subjects] is appreciably higher than the incidence of the disorder in control groups or in the population at large."

Studies of twins, by Rosenthal and many others, reflect similar findings. Identical twins, with identical genes, should develop the same genetic disease more often than non-identical twins. If this were true in even a small percentage of the cases, it would bolster the genetic thesis. A review of such studies, says Rosenthal, shows that this is the case approximately 50 percent of the time. Likewise, children of schizophrenic parents should have a higher incidence of the disorder, even when they are adopted and reared by non-schizophrenic parents. This also has been shown. "Thus," says Rosenthal, "all the major evidence points to the implication of genetic factors in this disorder, and this conclusion now finds common acceptance."

But common acceptance is not universal acceptance. For one thing, the disease has not been found in the chromosomes of a schizophrenic's parents. In *Genetic Factors of Schizophrenia* (see p. 55), Arnold R. Kaplan of the Cleveland Psychiatric Institute summarizes more than 50 years of research. None of the proof, he points out, has been conclusive.

Fifty years ago the thalidomide disaster would probably have been seen as genetic. Now it is known that the human fetus can learn or can be conditioned. So, schizophrenia could also be the result of prenatal trauma (especially during the last trimester), perinatal or immediate postnatal trauma. According to Virginia Johnson, Los Angeles clinical psychologist, nutritional deficiency, anoxia, microcirculatory collapse, drugs or even damage by forceps could be responsible for the disease. If this were the case, schizophrenia would be congenital but not genetic. Sarnof Mednick, working along these lines, studied the hospital records of 20 mentally ill children in Denmark. He found that 14 of them had suffered serious prenatal or birth complications (SN: 7/4/70, p. 15). Findings based on such studies, and her own observations of perinatal effects prompt Johnson to argue that there is every reason to explore early conditional factors for schizophrenia in greater depth.

In fact, no specific genetic theory in regard to schizophrenia has been established. With respect to the mode of genetic transmission, some investigators have advocated a single-gene theory involving dominance or partial dominance. Some have advocated a theory of recessiveness. Still others support two-gene theories with both genes dominant, both recessive or one dominant and the other recessive. None of these genetic theories has been clearly shown, but it is also very hard to get evidence for the fact that the individual did not have any genetic predisposition, says Rosenthal. "In both family and twin studies," he says, "the possible genetic and environmental factors are confounded, and one can draw conclusions about them only at considerable risk."

One possible method of avoiding this risk is by saying that only some forms

of schizophrenia are genetic. Process schizophrenia is a chronic form of the illness. Reactive schizophrenia is an acute form from which an individual recovers rather quickly and without any noticeable psychological deficit. "We have some evidence to the effect that the reactive form is not a genetic form of schizophrenia," says Rosenthal. The Europeans say it is not schizophrenia at all. They call it schizofreniform psychosis or psychogenic psychosis. But Rosenthal says he does not come down too hard on this theory because the data are insufficient and the number of subjects studied with this in mind is still small.

Even if this theory were accepted, it would not apply to all forms of schizophrenia and would be little more than a compromise. Until either the nature or nurture hypothesis is proved, the controversy will remain at a deadlock. New research presented at the recent meeting of the American Psychiatric Association points to where grounds for some sort of compromise may lie.

Rosenthal and Paul H. Wender of the NIMH, Seymour S. Kety of Harvard University and Fini Schulsinger of the City Hospital in Copenhagen, Denmark, set out to examine two different behaviors that have often been linked to schizophrenia, and "to show how it is possible by the proper selection of subjects to demonstrate that one of these behaviors has a genetic locus and that the other one has as its etiologic locus a type of parental rearing."

The first behavior they studied was migration, because it is a naturally occurring behavior over which the investigator has no influence. Previous migration studies seemed to indicate that migrants tend to have a higher rate of schizophrenia than non-migrants. Some said this was due to the great stresses migrants endure, others said the migrants had a schizoid character to begin with—possibly hereditary. But these studies usually compared foreign-born subjects to non-migrant subjects. To avoid this type of comparison Rosenthal and his co-workers selected and compared 659 subjects in Denmark before any of them emigrated.

Among adopted-away offspring of schizophrenic parents, the researchers found that 1.92 percent emigrated, compared with 8.5 percent of adopted-away offspring who did not have a schizophrenic parent. Of 56 children born and raised by a schizophrenic parent none emigrated. Of the adoptees who did not have a parent in the schizophrenia spectrum but who were raised by such a person, 7.55 percent emigrated. Comparing all groups in the study, the researchers found that 1.94 percent of those sharing schizophrenic genes migrated while 7.45 percent of those with no such blood relationship migrated.

The only factor involved in selecting the groups was biological relatedness to a schizophrenic. And in two of three of the groups there was no first-hand association with the schizophrenic relative. Therefore the researchers say they were forced to draw the conclusion that the difference between emigrating and not emigrating was related to the genes shared with the schizophrenic—implying that the disease is genetic. They add, however, that this study gives no information that bears on the stress theory.

The second type of theory studied was reaction time. Previous studies have shown that this measure is a simple, consistent method of discriminating schizophrenics and controls. Four groups were selected from 199 subjects. Two groups shared genes with a schizophrenic parent and two did not. Two groups were reared with a schizophrenic and two were not.

In the reaction-time procedure the subject was told to respond as quickly as possible and to ready himself for each trial. A tone was the stimulus, preceded by a flash of light and a varied or regular preparatory interval. Two kinds of response were used; one was a manual finger lift from a depressed key, the other a verbal uttering of a nonsense syllable.

"Since it is reasonable to assume that genetic factors do influence reaction-time performance," said Rosenthal, "we thought that we might find some relationship between having the schizophrenic genotype and poorer performance on reaction time tests." But this was not the case. The genetic hypothesis was not proved. Those subjects reared by a schizophrenic parent, whether related or not, had the slower reaction time on all tests. "This finding, like the one on migration," says Rosenthal, "had not been expected." Perhaps if the researchers had looked for conditional factors very early in development as Johnson suggests, the results would have been even less predictable. With all of these options and implications a person could go crazy just thinking about schizophrenia.

In any event, the results of these and thousands of studies have been conflicting and could be used to bolster either side of the hereditary-environment argument. Or, they could lead to a multivariable conclusion. Says Rosenthal, "Genetic influences are an important factor, perhaps a necessary one, in the development of schizophrenia, but environmental influences are also important." In other words, a person might have to have the genetic predisposition to develop the illness which could be precipitated by various kinds of stress.

Genetically minded scientists will continue to look for the schizophrenia chromosome and psychodynamically minded investigators will continue to try to elucidate the psychological and biodynamic factors responsible for the illness. But at least, research cannot be restricted solely to the gene theory. □