Nevertheless, Holzman and Matthysse propose that a "latent trait" exists for both schizophrenia and a possible biological marker for the disease—poor eye tracking. The researchers find that about 65% of schizophrenics (as opposed to 8% of the normal population), and about 45% of their first-degree relatives visually follow a moving object in interrupted movements rather than in a smooth, fluid motion.

Holzman, Matthysse, and their colleagues have just completed a study of eye tracking in two generations of offspring of schizophrenic twins. "In the branch of the family in which the gene is being transmitted, we predicted that about 30% of the people would show poor eye tracking, and that is what we found," says Holzman. This does not mean that everyone with poor tracking carries the gene for schizophrenia. "We think that poor eye tracking is a manifestation of the underlying disease process in those families," says Matthysse. "What we have really shown is that a simple genetic model—with a single dominant gene—fits the data surprisingly well."

Questions remain about poor eye tracking as a biological marker for schizophrenia, however. Although Nikki Erlenmeyer Kimling of the New York State Psychiatric Institute supports poor eye tracking as a potential marker, she is "worried that it sometimes doesn't occur in the patient when it does occur in a relative." For a trait to qualify as a good marker, she says, it must exist before someone ever shows psychotic symptoms of schizophrenia, be found at times between episodes, and indicate who is at risk for the condition. These criteria are not fulfilled by poor eye tracking.

Lynn DeLisi of NIMH points out that poor eye tracking is not specific for schizophrenia; people under the influence of certain drugs such as alcohol or barbiturates and patients with Parkinson's disease, multiple sclerosis, and certain brain lesions also track poorly.

The failure of the inheritance data to explain a cause for schizophrenia leads other researchers to seek possible nongenetic causes. For instance, Crow suggests that a retrovirus could infect healthy individuals, which might help to explain the unusually high prevalence of schizophrenia. If such a virus incorporates into the human genome, it could be passed from one generation to the next and account for the apparent heritability of schizophrenia.

The list of putative causes for schizophrenia is long and inconclusive. In the absence of hard evidence for any "viral hypotheses" of schizophrenia, some advocates point to data that slightly more (54% of the total) schizophrenics are born in winter or spring

A Top Priority at NIMH

Schizophrenia—or, more accurately, the schizophrenias—is the "cancer" of the mental illnesses. But, unlike cancer, it is still the object of public stigma and ignorance, and no "war" has been mounted against it. Whereas the government spends $300 on research for every cancer sufferer, the comparable figure for schizophrenia is about $17. Since the disease, which afflicts 1% of the population, is not fatal, lifetime costs of care are staggering. The Institute of Medicine has estimated that treatment and lost productivity cost the country $48 billion a year.

The National Institute of Mental Health (NIMH) is now trying to make schizophrenia research a top priority. The reorganization of the institute 2 years ago was effected mainly with an eye to emphasizing research on the major mental illnesses, and extramural research and training programs are now combined in the Schizophrenia Research Branch, headed by Samuel Keith, within the Division of Clinical Research. The staff has been more than doubled, to 13. A new clinical research lab headed by Daniel Weinberger is planned for the intramural research division. In addition to the Clinical Research Center at the University of California (Los Angeles), two new centers devoted to schizophrenia research have been designated, at the University of Maryland and at Long Island Hillside Hospital.

Congress tacked on $5 million to the fiscal 1987 research budget to be targeted to schizophrenia, making for a total extramural commitment of $20.4 million in addition to $10.1 million for intramural research. The fiscal 1988 presidential budget would keep the funding steady despite a 5% cut in the rest of the NIMH research budget. According to Keith, though, the field could readily absorb a tenfold increase in funds because of the rapid advances in brain imaging and biochemistry that have occurred within the past 5 or 6 years.

Until now, says Keith, schizophrenia research has been "something of a cottage industry." Now, he says, it is time to "address it in a major science way." Scientific leads have been a long time coming, in part because of the grip of psychoanalytic theories of mental illnesses which did not loosen until the 1970s when the revolution in biological psychiatry finally unseated psychosocial factors as the primary etiological suspects for schizophrenia. The political climate has also changed, with the rapid growth of organizations of the families of the mentally ill. The increase in the homeless population, one-third to one-half of whom are believed to be schizophrenic, has also made the problem painfully visible.

Developing a cadre of trained and committed schizophrenia researchers is still a problem. As Keith notes, schizophrenics are a specially difficult population to work with. For many years, the disease was regarded as hopeless and researchers were more attracted to the fast-breaking developments in the chemistry and treatment of emotional disorders.

NIMH convened a meeting in 1985 on incentives and disincentives for schizophrenia research careers where researchers agreed that "an overwhelming problem is the lack of a comprehensive theory," the development of which has been stymied by the "clinical and biological heterogeneity" of the disease. The dopamine theory is useful but by no means covers all the bases, as evidenced by the fact that 20% of sufferers do not respond to antipsychotic drugs. Researchers said the "nonspecificity" of many findings make other areas more intellectually satisfying. Alzheimer's disease, in particular, looks more promising to those wanting to make a career in brain research. (In 1980 the budgets for schizophrenia and Alzheimer's were comparable; now the Alzheimer's budget is double that for schizophrenia.)

Getting good research subjects is difficult. Schizophrenia, being chronic and financially debilitating, is not treated as often as is, for example, depression, in academic settings. This has made for a separation of clinical care and academic research. Keith says subjects are needed both at the "front and tail ends." That is, researchers need to study the chemistries of schizophrenics while they are still "drug virgins," which means that a major effort has to be made to refer patients to research centers before treatment. At the tail end are the chronic, treatment-resistant patients who end up in state hospitals and who rarely become research subjects.

Modest increases are being made in support for manpower development in schizophrenia research. But Keith says "people are still skeptical, they fear the spigot will be turned off again—they need to expect a stable base. It will take time." ■

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