Prenatal and birth complications linked by schizophrenia research

Schizophrenics' abnormal autonomic reactions and low tolerance for stress may be due to brain damage caused by anoxia

by James Moriarty and Lawrence Massett

Schizophrenia research has been confounded as much by the ambiguous results of poorly designed research as by the complexity of the disorder itself. Typical research projects on the etiology of schizophrenia have consisted of pooling a sample of mental hospital patients and then relying on interviews and questionnaire techniques to investigate possible causative factors.

A further difficulty involved in study of the disease, particularly in long-term studies, has been the highly unstable nature of schizophrenics. Researchers who start with a sample of 100 subjects are fortunate to be able to locate 20 of them five years later. Schizophrenics are often highly transient and notorious for not leaving forwarding addresses.

Eight years ago Dr. Sarnoff Mednick, presently at the New School for Social Research in New York, started a heavily funded research program designed to obviate these problems. Dr. Mednick, an experimental psychologist, was appalled at research designs traditionally employed in schizophrenia studies. In order to avoid the ambiguity problems entailed in an after-the-fact examination of the origins of schizophrenia, he designed a prospective study. In other words, he is studying schizophrenics before they become schizophrenic.

Dr. Mednick also took care to design a study that would retain its sample 20 years after initiation. He found a Danish population that was stable. Because Denmark is a small country with a housing shortage, the population is relatively nontransient. Furthermore, if citizens are to receive benefits from the National Sickness Association, they must report any change of address immediately.

In 1962 Dr. Mednick and a Danish psychiatrist, Dr. Fini Schulsinger, began an intensive examination of 207 children judged to run a high risk of becoming schizophrenic at some point in their lives. This judgment was based, among other things, on the fact that children of schizophrenic mothers are disposed to develop the disorder. A low-risk control group of 104 subjects was identified. The groups were matched on the variables of age, social class, education and geographic residence. An equal percentage of each group was living in institutions.

On the basis of other research, Dr. Mednick estimates that half of the high-risk children will develop some form of mental illness. About 30 percent of those who become mentally ill will be schizophrenic. Only 10 percent of the controls are expected to develop any mental disorder. Dr. Mednick intends to make intensive studies of groups of 20 as they become mentally ill.

The first group of 20 high-risk children was identified as mentally disturbed a year ago, seven years after the project's inception. Although not all 20 were diagnosed as schizophrenic, there was no question about the fact that they were all more than mildly disturbed; 13 of them had already been admitted to psychiatric hospitals. Drs. Mednick and Schulsinger combed the results of their earlier examinations to see what factors distinguished the children who became disturbed from those who remained normal.

For this purpose, the researchers compared the 20 high-risk children who had become disturbed with 20 high-risk children who had actually shown health improvements since the initiation of the study. The groups were controlled for age, sex, social class and institutional rearing. Both groups were also compared to the controls.

The outcome of this investigation has led Dr. Mednick to propound a new theory on the etiology of schizophrenia. What is perhaps more important, it has provided a list of important characteristics that precede the onset of schizophrenia and may, as Dr. Mednick hopes further research will prove, make it possible to prevent the disorder.

Midwife and hospital records, for instance, indicate that 14 of 20, or 70 percent, of the sick children had suffered serious prenatal and birth complications. Only 3 of 20 high-risk children who were still normal and 7 of 20 controls had such complications.

The main significance of this finding, Dr. Mednick says, lies in its correlation with another group of data showing that the disturbed children were markedly abnormal in tests of their galvanic skin responses (GSR).

The GSR is a measure of electrodermal conductivity regulated by the autonomic nervous system, which is largely in charge of regulating the body's internal stress reactions. A person's galvanic skin response can easily be conditioned by classical Pavlovian methods. Such conditioning procedures were applied to all the children in the study, and Drs. Mednick and Schulsinger found that the children who afterward became sick conditioned rapidly, but deconditioned with extraordinary difficulty. Once the sick children had learned a conditioned galvanic skin response, they had a great deal of trouble unlearning the response.

The sick children, furthermore, did not become habituated to stimuli in the normal manner. The healthy children in the study displayed a gradual dulling of their galvanic skin response as a result of repeated stimulation. The sick children seemed to lack any such protection against overstimulation, and responded at least as rapidly and intensely to the last stimulus in a series as they did to the first.

In addition to this autonomic irritability, the galvanic skin response of the sick children also showed an anomalous tendency to return to a normal level immediately after stimulation. In normal subjects, when the galvanic skin response has been elicited, electrothermal conductivity stays above the base level for some time afterward; the stress reaction, in other words, requires a brief time to fade. But the sick children suppressed their autonomic stress reaction very quickly.

Taken altogether, says Dr. Mednick, these abnormalities of galvanic skin response in the sick children suggest a poorly modulated autonomic nervous system. "The stress system responds too fast," he states, "and, what's even more significant, it recovers too quickly." The picture of a stress system that both overresponds and shuts down fast indicates, Dr. Mednick argues, that the sick children may be unusually adept in learning avoidance responses.

In experimental psychology, an avoidance response is said to occur when a laboratory animal takes steps to avert some unpleasant event that has not occurred but which the animal expects. If a rat has learned, for example, that a blue light is regularly followed by an unpleasant shock, he may learn to press a lever turning off the light when it appears, thus avoiding the subsequent shock. An avoidance response is difficult to extinguish, for if the animal invariably turns off the light, he never has the opportunity to learn that the shock may no longer be in operation. The mere fact that he is not being shocked is enough reward for continuing the avoidance response.

A similar process, Dr. Mednick holds may be at work in schizophrenics. "The stress system of schizophrenics," he says, "may make it easy for them to learn avoidance responses." Burdened with an exceptionally ill-modulated autonomic system, potential schizophrenics may find even mildly uncomfortable situations far more stressful than ordinary people. But since they can supress their stress reactions quickly, they may learn to cope with unpleasant situations simply by shutting off their own sense of stress instead of learning to deal with it.

The relationship between the autonomic irregularities of the sick children and their histories of prenatal and birth complication may be due to a number of factors. Dr. Mednick suggests that lack of oxygen, which often occurs during such complications, may be a major cause of irregular autonomic modulation. There is evidence that such anoxia affects the hippocampus region of the brain, which in turn affects the functioning of the autonomic nervous system.

"Researchers have singled out particular brain structures as being selectively vulnerable to the effects of anoxia. These areas include most prominently the hippocampus," says Dr. Mednick.

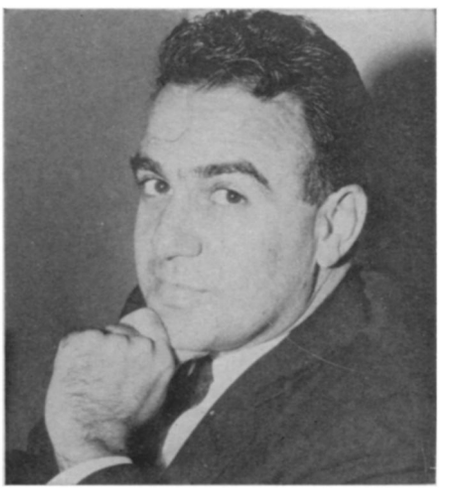
"Furthermore," the researcher continues, "if a sound hippocampus is a prerequisite for sound mental health, and if we can avoid prenatal and birth complications in high-risk populations, we may avert hippocampal change and hence reduce the probability of mental illness."

The researchers also note the possible involvement of poorly modulated hormonal secretions. This may indicate that psychopharmacological intervention at an early enough age to anticipate the onset of the disease would be beneficial.

This theory of schizophrenia etiology that emerges is admittedly speculative. Dr. Mednick and a Danish research team are beginning another study in which the children of normal parents and the children of schizophrenic parents will be matched for birth circumstances. "The new study," he says, "should make it possible to look more closely at the genetic-physiological interaction."

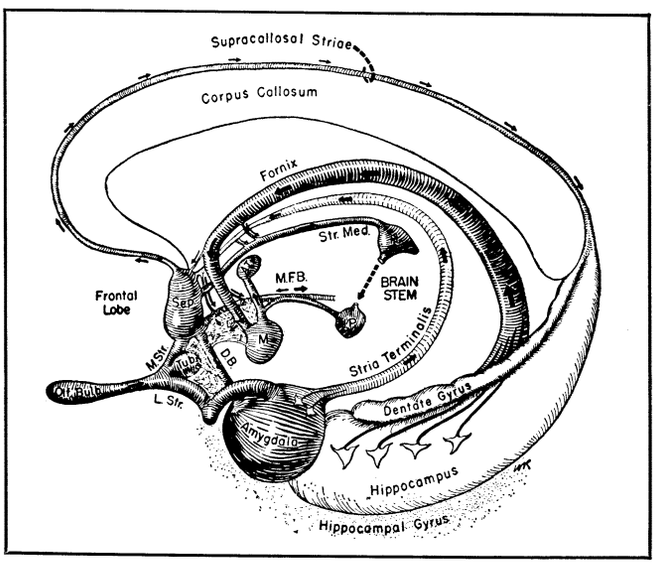
In cooperation with the World Health Organization, Dr. Mednick is now making plans for a project to be launched in Africa in the next few years aimed at detecting and treating children with a high risk of schizophrenia. The project will seek to identify children around the age of three who exhibit the psychological and physiological symptoms that Drs. Mednick and Schulsinger have found to be characteristic of children who later become mentally disturbed. At special nursery schools, the children will be treated with a combination of drug and behavior therapy.

World Health officials have not decided just what form the psychopharmacological treatment will take, but Dr. Mednick says the behavioral treatment will consist of encouraging the children to deal with stress in a realistic manner. Positive adaptive behavior instead of schizophrenic withdrawal will be emphasized as a response to stress situations. "We will try to get the children to focus on making approach responses instead of avoidance responses," he says. "The nursery school," he adds, "may be the preventive treatment center of the future." □



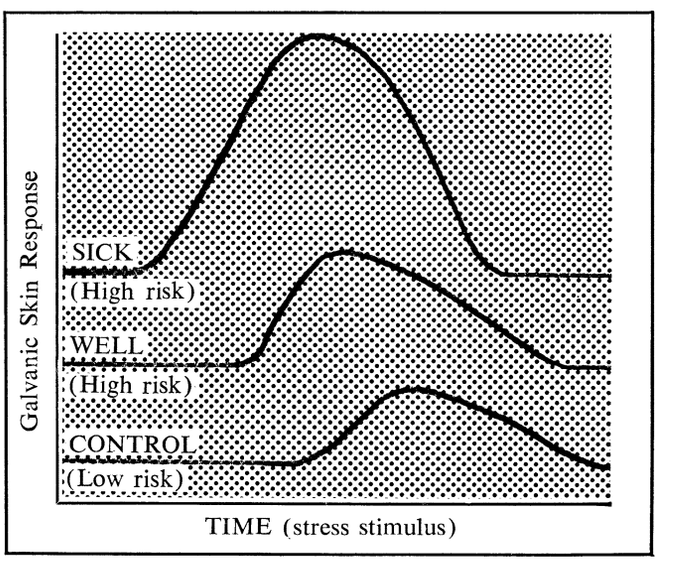
New School

Mednick: New schizophrenia theory.



Psychosomatic Med.

Anoxia may damage hippocampus region of the brain.



Mednick/R. Trotter

Stylistic comparison of GSR conditioning rates.