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ABSTRACT

The booklet reviews the findings of a Danish longitudinal study involving 200 children (10-20 years old) at risk for schizophrenia and 100 controls. The views of the study's investigator, S. Mednick, regarding the schizophrenic Ss' learned avoidance and heightened physiological response to stress are explained. Other findings discussed include that most schizophrenic Ss had prenatal and birth difficulties and had been separated from their parents early in life. Evidence that the schizophrenic process in women may differ from that in men is considered. It is explained that Mednick views schizophrenia as an "evasion of life" which is a learned behavior: he suggests that the schizophrenic learns to avoid stress or anxiety by switching into irrelevant thinking. A second long-range investigation underway in Mauritius is reported to be examining the influence of the autonomic nervous system on children's behavior. (CL)

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A LONG-RANGE STUDY OF SCHIZOPHRENIA

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A Long-Range Study of Schizophrenia

by Herbert Yahraes

Throughout the world, some 25 or 30 teams of researchers are using a relatively new approach to try to isolate the causes of probably the most feared and fearsome of mental illnesses—schizophrenia.

The new approach is longitudinal research—research that follows people for many years, sometimes from birth to middle age or beyond, and tries to observe all the major influences affecting their lives. The eventual goal is to isolate from a host of factors just the ones responsible for mental illness.

Longitudinal research is costly and difficult, but it offers great hope that some day we shall be able to spot signs early in life of impending trouble and perhaps ward off the threatened disease. Longitudinal studies are in contrast to retrospective research in which the investigator usually has to rely greatly on fallible memories.

The oldest of the long-range studies of schizophrenia, the one with the most findings, began in 1962. Its subjects are Danes at high risk for schizophrenia because they have schizophrenic mothers. This account of it is offered as an indication of the effort required for a comprehensive study on one of the most perplexing problems of mental health, but a problem which—through studies like this and through laboratory research—is beginning to yield its secrets.

Conducting the study are Sarnoff A. Mednick, a well-known American psychologist, and Fini Schulsinger, a well-known Danish psychiatrist. Mednick originally planned to

study Detroit children and their parents but found that they probably would be difficult to follow for 20 or 25 years, as planned, because the Detroit population frequently moves. In Denmark, people tend to change residence much less frequently than in the United States. Denmark offers researchers another advantage: The government's excellent population records include information on every person's prenatal and birth situations and subsequent mental and physical health.

Mednick and his fellow workers began by selecting 200 children whose mothers were schizophrenic. They also selected about 100 controls—children considered at low risk because no family member in three generations had been hospitalized for psychiatric illness. The children in both groups were between 10 and 20 years old when the study began, and none had had a mental breakdown. However, the high-risk children thought less well of themselves, had greater difficulty in making friends, were more tense, sensitive, nervous, and schizoid (a condition marked by shyness, seclusiveness, and, frequently, eccentricity), and they had significantly lower IQs. Almost 25 percent of them, compared to 1 percent of the controls, were considered to be poorly adjusted.

According to their teachers, "the high risk children seemed to react to excitement by withdrawal." The words are those of psychologist Norman Garmezy, who is involved in a longitudinal study himself and has helped to summarize and evaluate such investigations for the National Institute of Mental Health. Further, the high-risk boys, compared to the controls, were more aggressive and interrupted class sessions more often. "Such findings," Garmezy notes, "are congruent with those of retrospective school record studies of individuals subsequently diagnosed schizophrenic."

A difference in the ways the two groups responded to stress was indicated by the galvanic skin reflex (GSR). The GSR, widely known because it is used in lie-detector tests, is a momentary decrease in the skin's electrical resistance in response to stress. To understand the importance Mednick attaches to this result and to a related finding some years later, let us consider how this investigator views schizophrenia.

Mednick holds that schizophrenia, to a certain extent, is an "evasion of life" and that this evasion is learned. He offers as an example a laboratory rat that is placed in a piece of equipment called a shuttle box.

The rat is first placed in compartment A, and a bell is rung. "Ten seconds later the floor of compartment A is electrified. The rat leaps up, runs around, defecates, urinates, and eventually runs into B and safety. After perhaps 10

trials, the rat will learn to avoid the shock by running into B at the sound of the bell."

What produces this so-called avoidance learning? One obvious and critical factor, answers Mednick, is the shock—and, soon, the bell all by itself—which produces fear. The more fear produced, the faster the rat learns to avoid the pain. Another critical factor is the reward—a reduction of fear—that the rat gets by running into the safe compartment.

The value of that reward or, in psychological terms, "reinforcement" depends both upon its size and the speed of delivery. Under Mednick's hypothesis, this is where the autonomic nervous system comes in; because the speed with which the fear is reduced depends "in large part on the rate at which the autonomic nervous system recovers from a fear state to a normal level. The faster the rate of recovery, the faster the delivery of the reinforcement and the greater the reinforcement."

For a rat that recovers very slowly, Mednick explains, the difference between the shock and the safe compartments will be lessened. So will the rat's reward for jumping from one compartment into the other. However, "if the rat has abnormally fast autonomic recovery, his reinforcement will come abnormally quickly," and he will learn abnormally quickly how to avoid the pain. Abnormal speed in responding to the danger signal, the bell, and in the recovery of the autonomic nervous system function, then, "are aptitudes for learning avoidance responses, just as nimble fingers and absolute pitch provide aptitudes for learning to play the violin."

Now, let us consider the human. He or she does not have to run, or move at all, to avoid an anxiety-producing stimulus. A young person or an adult can learn to avoid stress, according to Mednick, simply by thinking thoughts that are not relevant to the anxiety-producing situation. In effect, the irrelevant thoughts will remove that person from stress. The faster a person's recovery system works, the more likely that he or she will feel rewarded for the irrelevant thoughts; and the more likely such thoughts will be elicited the next time the individual faces an anxiety-arousing situation. "Over years, the pre-schizophrenic will learn more and more of these avoidant thoughts." By the time the thinking has become predominantly evasive, "a clinician will be able to note the thought disorder and will diagnose schizophrenia."

In other words, Mednick hypothesizes that, if a person, because of the way his or her autonomic nervous system behaves, responds to anxiety with abnormal speed and to an abnormal degree, and if the system also gets back to normal with abnormal speed, that person will have an aptitude—a predisposition—for learning to avoid anxiety simply by

switching into irrelevant thinking. However, the predisposition will cause trouble only "in *response* to unpleasant environments or noxious thoughts." A person who is treated kindly is far less likely to evince distressing overexcitement of the autonomic nervous system "and will have relatively little provocation to learn a massive pattern of avoidant responses." Mednick sums up his idea: "The development of schizophrenia depends then on an interaction of reactive, sensitive, and quickly recovering autonomic nervous systems and unkind environments."

This investigator offers what he considers strong evidence to support his views. The children in the longitudinal study who were at high risk to schizophrenia, it was noted earlier, responded differently to stress, as indicated by the galvanic skin reflex. Two 5-year followups have been made so far, first when the subjects were 20 years old, on the average, and then when they were 25. By the time of the second followup, there had been two momentous changes. First, eight of the young people in the high-risk group had died, at least four by suicide, but none of the controls, or low-risk group had died. Second, 13 of the high-risk subjects had developed schizophrenia, and 71 showed evidence of schizoid or paranoid personality disorders or other so-called borderline states.

In contrast, only one "control" had developed schizophrenia—and, it was later discovered, this person should not have been included in the control group: Unknown to the investigators, the mother of this "control" had been hospitalized for treatment of psychotic episodes before the study began. Moreover, only five persons among the controls had one or another of the borderline conditions; and 30 percent of the controls were judged to be entirely free of any mental disorder, as compared with only 13 percent of the high-risk group.

In electrodermal measures, Mednick and his associates found significant differences between high-risk individuals who had broken down and those who had not and also between those who had become ill and the controls. The rate at which the autonomic nervous system returned to normal after stress, as measured at the start of the study, predicted "very well" those children who would develop schizophrenia during the next 10 years, particularly those who would have hallucinations, delusions, and thought disorder. The faster the return to normal, the greater the likelihood of schizophrenia. In a separate study, Mednick and his co-workers have found that this recovery time is significantly influenced by heredity.

In line with the Mednick group's findings, numerous other studies in the United States, England, and Sweden suggest that heightened psychophysiological responsiveness and fast

recovery are important characteristics of chronic, withdrawn schizophrenics. In one of these studies, for example, the stress was the unpleasant effect of a puff of air on the eyeball. The puff was preceded by a warning signal. Schizophrenics learned faster than other people to close an eyelid at that signal and thus to escape the stress. And the schizophrenics whose behavior was the most withdrawn and avoidant learned the fastest.

A cautionary note is in order. Many investigators question —in the words of research psychologist Garmezy—"the appropriateness of using deviant psychophysiological functioning in children as a criterion of risk." In fact, Mednick's basic hypothesis that a predisposition to schizophrenia is created by an autonomic nervous system that is highly reactive to stress is by no means universally accepted. In question are not the findings of the skin-conductance tests but the interpretation of them.

The Mednick team found also that:

- Most of the sick group had been involved in prenatal and birth difficulties.
- The mothers of the children who became schizophrenic had developed schizophrenia themselves at a younger age than the other mothers.
- Most of the schizophrenic children, in contrast to the others, had been separated from their parents early in life, mainly because of the mothers' illness.
- The children who became schizophrenic were extremely disturbing in school, easily became angry, and were violent and aggressive.

One finding was surprising, though there have been hints of it in a few other studies: When the investigators grouped their subjects by sex, they found that—for reasons not yet known—*all the results given above applied to males but not to females.* There was one exception: The development of schizophrenia in girls, as in boys, was significantly related to the age of onset of the same illness in the mother—that is, the earlier the mother developed schizophrenia, the more likely that her children would develop it, too. In the boys but not in the girls, "This relationship seems to be almost completely explained by the separation from parents which follows the mother's early onset of illness."

Mednick and his associates are also following 200 children in Mauritius, an island country in the Indian Ocean. The children were chosen largely on the basis of their response to the skin conductance test. More than half of them show a very fast recovery from stress. Half of the children are attending special nursery schools; the others are the controls.

These children were 3 years old when first examined. The children with *slow* electrodermal rates, Mednick reports,

were those who did not cry in the laboratory and were less anxious about the testing. The children with fast recoveries showed not only more anxiety during the testing but also more aggressive and disturbing behavior in the nursery school. It will be interesting to see if these, as the research team hypothesizes, are the ones at high risk to schizophrenia.

From the standpoint of activity in the nursery schools, Mednick and his associates find that both groups of children—those with a very fast rate of recovery as well as the others—are functioning essentially well. Children with a very fast recovery rate improve most in attempts to initiate friendly contact. In contrast, those who respond at the average speed improve most in solitary constructive play. These observations make it evident to the researchers that the functioning of the autonomic nervous system, the criterion for selecting the subjects in the study, has some influence on a child's behavior.

In sum, the Mednick group is conducting two long-range investigations. The investigation in Denmark—presently supported by the National Institute of Mental Health and at one time supported by the Foundation for Child Development—has already confirmed that schizophrenia has a strong genetic base and that pre-schizophrenic boys tend toward violent and other disturbed behavior in school. Moreover, the research has found evidence that the schizophrenic process in women may differ from that in men; in other words, some of the factors which seem to bear upon the development of the disease in one sex may differ from those bearing upon it in the other. At first glance, this finding appears to make the researchers' task more complex than ever. But eventually it may help to clarify the role of apparently causative circumstances.

Because schizophrenia strikes in adolescence or later, the Mauritius study may have no important findings for another dozen years. However, it is among the newest of the longitudinal studies on schizophrenia; which, taken together, constitute a giant step toward understanding this mental health enigma.

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