Reported is a research program to observe children at high risk for schizophrenia and explore possibilities of prevention. Characteristics of the high risk group (n=207) observed during 1962 are discussed, and a theory which suggests that schizophrenia is an evasion of life is explained. Among results of a diagnostic assessment conducted 10 years later with high and low risk samples (20 to 30 years old) were that all of the mothers of the high-risk Ss were seriously schizophrenic, that the birth of the schizophrenic group was relatively difficult; and that ANS (autonomic nervous system) recovery rate was found to predict very well to later schizophrenia. Separate analyses were conducted for male and female high risk individuals to examine the effects of seriousness of illness of the mother, separation from parents during early life, pregnancy and birth complications, and ANS recovery and responsiveness on development of schizophrenia. Some tentative reflections regarding sex related findings are offered. It is concluded that the form which schizophrenia takes in men and women may be different along with withdrawal-activity dimension and that these differences may be related to the hypothesized role of ANS factors in the learning of avoidance-withdrawal. Tables and charts with statistical data are provided. (SBH)
Schizophrenia in High-Risk Children: Sex Differences in Predisposing Factors

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In a letter to Lancet, Gruneberg (1976) has called attention to some unforeseen consequences of the healing profession's increasingly sophisticated technology of treatment. Progress in our capability of maintaining life and treating disease has actually produced an increase in the population of the chronically ill. This has, in turn, increased the general level of desperateness of need for treatment in the population. The response to this desperateness has been an increased emphasis on treatment-technology research. In this paper we will argue that in order to reduce human suffering, some increasing proportion of society's resources should be devoted to prevention-related research.

The emphasis on prevention will be critically important no matter what the ultimate causes of mental illness may be. If the causes are biochemical or neurophysiological deviance, these may prove to be irreversible; what is even more likely, however, is that the learned reactions to any biological inadequacy or environmental perversion may become a fixed habit by the time the condition is well-established and recognized. These fixed habits may be rather resistant to treatment even if the original cause is removed. These considerations, plus the difficulties in interpretation of research with patients already schizophrenic, (Mednick and McNeil, 1968) resulted in the emphasis of our research on efforts in prevention.
The overall high risk-intervention research plan

From the beginning it was clear that preventive interventions would very likely be, at least psychologically, invasive or intrusive. That is, they would demand time and investment from the subject-participants. (In contrast to preventive methods such as fluoridation of the water supply.) A consequence of this is that one could not plan or total population efforts in prevention such as the smallpox or polio vaccines. The research strategy would have to begin with the identification of individuals at especially high risk for psychiatric conditions, and the enlisting of their co-operation in research on prevention. In this manner the interventions will be offered only to those with the greatest need.

This research program was first proposed in 1960. At that point it was planned "to test and interview a group of normal children in the Detroit area. From these tests and interviews we shall predict which of these children will become schizophrenic..... we have decided to select a group in which the prevalence rates are considerably elevated.... individuals who have one or two parents who have been schizophrenic. If our predictions prove to be supported, we are then in a position to do research which is aimed at the prevention of schizophrenia. We might observe a normal population with our tests, detect those individuals who
are potential schizophrenics and then explore the possibilities of intervention." (Mednick, 1960, page 69.)

In accordance with this overall plan, in 1962 we intensively examined a group of 207 children at high-risk for schizophrenia. (They have schizophrenic mothers.) We also examined 104 control subjects. We followed this group until 1967 when 20 of them evidenced a variety of psychiatric breakdowns. In good agreement with the general theory guiding this research, an autonomic nervous system (ANS) variable, (fast recovery rate) proved to be the best discriminator of the breakdown subjects from their carefully chosen high-risk and low-risk controls. We then took this "best discriminator" to Mauritius where we examined the ANS functioning of all of the three-year old children in two communities (1,800 children). In accordance with our theoretical position (Mednick, 1958; Mednick and Schulsinger, 1973) we selected out the 6% of the 1,800 (108 children) who evidenced the fastest recovery and greatest responsiveness in the population. Half of these individuals, along with controls, were then placed in specially established and organized nursery schools. The other 54 children were considered community controls, and were only identified in our files. (For the first description of this project see Schulsinger, et al, 1975.) In a companion paper (with Peter H. Venables as first author) we shall pick up the thread of the prevention project in Mauritius and relate the promising outcomes observed.
The 20 breakdowns in 1967 ranged from schizophrenia to extreme schizoid states to antisocial behavior. The follow-up of the Copenhagen high-risk subjects continued in order to see whether ANS recovery and/or other variables would predict specifically to later breakdown with schizophrenia. The results of these follow-up activities will form the basis of this paper.

The Copenhagen 1962 high-risk project

A check on the psychiatric-genetics literature. When we began in Copenhagen in 1962 it was clear to us that we were perhaps relying too heavily on American and German reports that the probability of schizophrenia was relatively high among children with schizophrenic mothers. We encouraged the efforts of Dr. Niels Reisby to conduct a comparable Danish study; his finding of a 12.7% risk (corrected) of schizophrenia for children with schizophrenic mothers fell within the range of previous findings. From the Reisby article (1967) we noted that, by the age of 25 years, 52% of his sample of children of schizophrenic mothers had been admitted at least once to a mental hospital. This fact determined the date of our clinical follow-up in 1972.

Method of procedure. In 1962 we intensively examined 207 children at high risk (HR) for schizophrenia. They have schizophrenic mothers. We also assessed 104 children...
at low risk (LR) for schizophrenia. The identifying characteristics of these samples are given in Table 1. Table 2 presents the list of examination procedures. Some of the measures which will be critical for our later remarks stem from the interview made by a social worker with the individual responsible for the rearing of the child. From this interview we derived information on the social status and the intactness of the family and retrospective comments on the child's behavior as an infant and small child. From the files of the Demographic Institute in Risskov and the mother's hospitalization record we extracted information relating to the form and seriousness of her illness. Danish midwives attended the birth of our subject population and prepared a written report on the pregnancy and delivery which we have coded. The psychophysiology examination yielded two important channels of information. One on the heart rate response, and the other on electrodermal responding. We shall center our discussion on the electrodermal behavior.

The first 20 psychiatric breakdowns. Following the intensive examination in 1962 an alarm network was established in Denmark, so that most hospital and all psychiatric admissions for anyone in this sample would be reported to
us. The number of reports of serious psychiatric or social breakdowns reached 20 in 1967. Very brief summaries of their case stories are given in Table 3. We then looked

Insert Table 3 about here

back to our data from 1962 to find characteristics that distinguished the schizophrenia breakdown individuals from carefully matched HR and LR controls. The most important characteristics distinguishing the Sick Group from the controls are given in Table 4.

Insert Table 4 about here

We shall call attention to a few of these characteristics. 1) The Sick Group suffered considerably more early separation from their parents than the two control groups. 2) Rather than the classic textbook picture of the preschizophrenic child, the Sick Group subjects were disciplinary problems, domineering and aggressive in their classroom behavior. 3) While a number of psychophysiological variables predicted to their Sick Group status, the one which was the best discriminator was the rate of recovery from momentary states of autonomic imbalance. 4) The Sick Group evidenced considerably more pregnancy and delivery complications. An interesting sidelight with respect to these peri-
natal events is the fact that the high-risk group which had not suffered breakdown evidenced fewer perinatal difficulties than did the low-risk control group. This suggested to us that perhaps there is a special interaction between the genetic predisposition for schizophrenia and pregnancy and delivery complications. It was almost as if in order for a HR subject to fare well, he needed a complication-free pregnancy and delivery. In the paper reporting the findings (Mednick, 1970), mention was made of the fact that there was a marked correspondence between the pregnancy and birth complications and the deviant electrodermal behavior. Almost all of the electrodermal differences between the groups could be explained by these perinatal difficulties in the Sick Group. The perinatal difficulties in the LR group were not as strongly associated with these extreme electrodermal effects. This further suggested that the pregnancy and delivery complications trigger some characteristics that may be genetically predisposed.

A theory of schizophrenia

This theory was first stated in 1958 (Mednick, 1958). A clinical formulation of the theory was stated in 1962 (Mednick, 1962). Schizophrenia is seen as an evasion of life. It is suggested that the syndrome of schizophrenia is learned on the basis of physiological predispositions, and that this learning takes place very gradually over a period of many years. The hypothesized physiological apti-
attitudes are very fast ANS recovery and ANS hyperresponsiveness.

The essence of this theoretical approach suggest that schizophrenia is a learned evasion of life. To understand the role of the ANS variables in this learned evasion we must first clarify our view of avoidance learning. Studies of avoidance learning have been conducted mostly with rats and mostly in shuttle boxes. The rat is first placed in compartment A; a bell rings and 10 seconds later the floor of compartment A is electrified. The rat leaps up, runs around, defecates, urinates, and eventually runs into compartment B and safety. After about 10 trials the average rat will learn to avoid the shock by running into B at the sound of the bell. Some rats learn this quickly, and some rats learn this extremely slowly. What factors might be important in the speed with which a rat learns this avoidance response? Our analyses of this situation are related to that presented by Mowrer (1960). One critical factor is that the rat must have a response of fear to the shock and must be capable of learning to transfer this fear response to the bell. The greater the fear, the faster his learning to avoid the shock. Another critical factor which perhaps is a bit less obvious is that when the rat runs into the safe compartment B, his avoidance response is rewarded by fear reduction. The value of a reward is directly related to its speed of delivery and to its magnitude. The faster and the greater the reduction of fear, the greater the re-
ward value. In the case of the rat in the shuttle box, the rate at which this fear is reduced depends almost completely on the rate at which his ANS recovers from a fear state to a normal level. The faster the rate of autonomic recovery, the faster the delivery of the reinforcement and the greater the reinforcement. If the rat recovers very slowly, then his avoidance response will not be rewarded very quickly, or with any great magnitude when he enters the safe compartment B. If, on the other hand, the rat has abnormally fast ANS recovery, his reinforcement will come abnormally quickly, and he will learn this type of avoidance response quickly. Thus, we have named two factors which are relatively independent (Lockhart and Lieberman, 1976) and which will help to determine the rate at which the rat will learn the avoidance response: 

1. level of ANS responsiveness, 2. rate of ANS recovery.

These two factors then will function as aptitudes for learning avoidance responses, in some ways analogous to the role of nimble fingers and absolute pitch in providing aptitudes for learning to play the violin.

Learning avoidant thinking. Running away is not the only form that an avoidance response can take. A human can learn to avoid threatening stimulation by simply thinking irrelevant thoughts. These irrelevant thoughts will, at least partly, remove him from a fear-producing stimulus. If he has fast ANS recovery and is highly responsive, the
avoidant thoughts will be richly rewarded and will increase in their probability of being elicited in the presence of anxiety. Other more complex and even more bizarre responses may be learned to avoid threatening or unpleasant ANS stimulation. Clinicians have shared the experience of approaching a chronic schizophrenic on the hospital grounds and precipitating a display of bizarre symptoms by simply saying "good morning". Note that if the environment does not elicit these ANS responses, or if the ANS responses are not threatening or unpleasant, avoidance learning will not occur.

Beginning in childhood and through adolescence an individual with a highly responsive and fast recovering ANS will have a tendency to learn more and more of these avoidant responses if he is faced with unkind environments. One of the critical life consequences for such an individual is the fact that this avoidance-learning will obviate the need, and thus the possibility, for him to learn more positive, "normal" manners of dealing with life's vicissitudes. It is perhaps this isolation from the experience of direct dealings with "life" which is responsible for the social helplessness and inappropriateness of the adolescent and adult schizophrenic.

The theory then suggests that the combination of an ANS that responds too often and too much and an abnormally fast rate of autonomic recovery provide an aptitude for
learning avoidance responses. If an individual is to become schizophrenic, he must possess both the ANS responsiveness and recovery characteristics. If an individual is rapidly, exaggeratedly and untiringly emotionally reactive, he may become anxious or even psychotic, but will not tend to learn schizophrenia unless his rate of recovery tends to be very fast. It also seems likely that an extraordinarily reactive ANS will only require moderately fast recovery, while an extraordinarily fast rate of recovery will only require moderate reactivenss. Both very high reactivenss and very fast recovery will result in a very heavy predisposition for avoidance learning and hence for schizophrenia.

Diagnostic Assessment, 1972

The Reisby study (1967) gave us reason to expect that at the average age of 25 years, we should expect to be able to diagnose approximately half of the eventual schizophrenics in the high-risk group. Thus, we initiated an intensive assessment of the high and low-risk samples in 1972 when they reached an average age of 25.1 years. (They ranged between 20 and 30 years of age.) The central goal of this re-assessment was the establishment of a reliable diagnosis and an evaluation of their current life status.

Method of procedure. The 1972 assessment consisted of psychophysiological and cognitive tests, a social inter-
view, and, most importantly, a battery of diagnostic devices. The diagnostic devices included a 3 1/4 hour clinical interview by an experienced diagnostician (H.S.), a full MMPI and the psychiatric hospitalization diagnoses and records where they existed. The diagnostic interviewer completed the Endicott and Spitzer Current and Past Psychopathology Scales (CAPPs, 1972) and the Present Status Examination, 9th edition (PSE) (Wing, Cooper and Sartorius, 1974). The interview itself was structured as a clinical procedure and not as a questionnaire.

The coded PSE and CAPPs materials were sent to New York and London; computer diagnoses were returned. Table 5 presents information on the results of our follow-up contacts with the subjects. Ten of the high-risk subjects have died in the course of the follow-up, seven by suicide, two by accidental causes, and one by natural cause. None of the low-risk subjects have died. This is a dramatic difference which we shall explore further in future papers. Of the ten, six died before the assessment began; three of the other four took part in the assessment. Thus, of the 201 high-risk subjects available for the assessment, 91% took some part in the interview (10 only had a home interview by the social worker). Of
the low-risk subjects 91 took part in the full interview, six took part in the home interview. Thus, 93% of the low-risk group has taken some part in the interview. Subjects are still trickling in for the assessment.

Table 6 presents identifying information on those who completed the full interview. The groups seemed to be well-matched with each other and with the total original sample with respect to age, sex, and social class.

Reliability of the diagnosis. The diagnosis of schizophrenia made by the interviewer is based on the presence of Bleuler's primary symptoms: thought disorder, autism, ambivalence, and emotional blunting as well as Bleuler's secondary symptoms: delusions and hallucinations. For a diagnosis of schizophrenia it was not necessary that all of these symptoms were observed at the time of the interview; they might also be drawn from the case history. In two separate papers (Mednick, et al, 1975; Schulsinger, 1976) detailed descriptions of the tests of the reliability of the diagnoses have been reported. For our purposes here, it is sufficient to say that across the two computer-derived diagnoses, the MMPI (analysed blindly by Professor Irving Gottesman) and the clinical diagnosis as well as an independent diagnosis arrived at by two Danish psychiatrists
listening to the audiotape of the entire interview for ten subjects, rather excellent diagnostic agreement was achieved.

The interview was, in part, coded in the form of a rather extensive series of questions. A very significant portion of these questions refer to symptoms of mental illness. It is interesting that one of the Danish psychiatrists listening to the audiotapes of these interviews had almost perfect agreement with the interviewer's codings of the CAPPS items. The codes for these items range from 1 to 6. In 91% of the items his coding was no more than one unit different.

Another indication of the reliability of the coding and diagnoses may be found in the two important measures of severity of illness resulting from the interview. At the conclusion of the CAPPS interview form, the interviewer is required to rate the severity of illness on a scale from one to six. Ratings of five and six only occurred for those who were diagnosed schizophrenic. This rating correlated .70 with a rating of severity derived from the PSE.

Results of 1972 assessment

Distinguishing phenotypic characteristics of those diagnosed schizophrenic
The interviewer diagnosed 13 schizophrenics in the high-risk group. In a previous publication we have compared these 13 schizophrenics with 29 borderline schizophrenics, 34 neurotics, and 23 high-risk subjects with no mental illness. This report (Mednick, et al, 1975) suggested that these high-risk subjects who became schizophrenic were characterized by the following factors:

1. All of the mothers of the high-risk subjects were seriously schizophrenic. The mothers of the children who became schizophrenic developed their illness at a younger age.

2. Most of the 13 schizophrenics had been separated from their mother and father and many placed in children's homes quite early in their lives. This stands in sharp contrast to the patterns in the other diagnostic groups.

3. The birth of the schizophrenic group was relatively difficult. The period of labour was longer and characterized by more complications.

4. The rearing social class of the schizophrenic group was not noticeably different from that of the other groups.

5. The school teachers reported that the schizophrenics were extremely disturbing to the class, evidenced in-
appropriate behavior, were easily angered, and violent and aggressive. They posed a disciplinary problem for the teacher.

6. ANS recovery rate (measured in 1962) was found to predict very well to later schizophrenia (Mednick, in press) and especially well to individuals suffering symptoms of hallucinations and delusions and thought disorder.

**Sex differences in factors predisposing to schizophrenia**

In considering these preliminary reports one factor seemed extremely striking. We were sensitized to this factor by a dissertation completed by Dr. Helen Orvaschel (at the New School for Social Research, 1976) on sex differences in high-risk children. Almost all of the findings we have listed above have been cited in the literature as being especially responsive to sex differences in schizophrenics. Gardner (1967) and Sobel (1961) have reported that the degree of mother's illness, for example, effects the level of schizophrenia in females, but not in males.

Posenthal (1962) has commented on the higher concordance for female monozygotic schizophrenics than for males. Male discordance in monozygotic twins with schizophrenia is twice as great as for females. While there are some sampling problems in these twin studies, such information might
suggest that schizophrenia in females is more genetically determined, and that schizophrenia in males has a heavier environmental weight.

With respect to the pregnancy and delivery complications, in our more recent high-risk study especially studying perinatal factors (Mednick, et al, 1972) we have found differential sex effects of perinatal complications. It is also well known that males are more vulnerable to pregnancy and delivery difficulties. Finally, aggressive school behavior has been shown by Watt, et al (1970) to be associated with later schizophrenia in men, but not women.

In view of the fact that almost all of the findings reported in the two preliminary reports mentioned above are highly sex dependent, we determined to conduct separate analyses of these variables for males and females.

**Hypotheses to be examined.** The analysis of the factors potentially predispositional to schizophrenia were conducted separately for male and female HR individuals. It was hypothesized that:

1. The seriousness of illness of the mother (as indicated by early onset) would be of significance for both sexes, but would be more important for women.

2. Separation from parents during early life would
be important for both sexes.

3. **Pregnancy and birth complications** would increase the probability of the development of schizophrenia in both sexes. Because of the male foetus' greater vulnerability to perinatal stress, we hypothesized greater effects for males than females.

4. **ANS recovery and responsiveness** would be involved in the development of schizophrenia.

In summary, we hypothesized that for female HR individuals the development of schizophrenia would be especially related to early onset of the schizophrenic mother's illness. In males we hypothesized that the perinatal variables would be especially predictive. In both sexes ANS factors and early separation were hypothesized as predispositional to schizophrenia.

**Method of statistical analysis:**

*Path analysis*

While a practical goal of this statistical analysis is to develop identifying characteristics of children who will later become schizophrenic, an underlying hope is progress toward an understanding of the etiology of schizophrenia. The problem is one of causation. Because we are barred in studies of the etiology of schizophrenia from
making use of the experimental-manipulative approach, it has been impossible for researchers in the field of schizophrenia to pretend to such causal statements. As Simon (1954), quoting Hume, has asserted, all we can ever observe is co-variation. Certainly for research in a naturalistic setting (such as this longitudinal project) this point must remain unchallenged.

Methods have been developed, however, in the field of genetics and later used extensively in the field of economics which allow for hypothesized causal models to be stated in mathematical form in a way that allows their agreement with observed co-variances to be examined. So while we can never completely validate or prove a "causal" statement, we can examine its expected consequences by examining the goodness-of-fit of hypothesized co-variances (i.e., generated under a hypothesized model) to observed co-variances.

In this analysis we are operating with variables which span the lifetimes of the individuals involved. We begin with the seriousness of the schizophrenia of the mother, examine perinatal factors, consider the intactness of their homes, see all this in the light of their socioeconomic status during rearing, the functioning of their autonomic nervous system and their sex. We know that many of these independent variables are intercorrelated. For example, the earlier the onset of illness of the mother, the more
separation from the mother the child experiences. Other, less obvious, intercorrelations also exist in these data. Therefore, multiple analyses of individual independent variables in relationship to the dependent variable, schizophrenia, run the risk of repeatedly a single or few common findings. Therefore, we chose a model in which all of the interrelationships are estimated simultaneously and all other intercorrelations are taken into consideration. We also foresaw the possible problems inherent in mediated effects. Thus, the seriousness of illness of the mother might not have any direct effects on her child's development of schizophrenia, but may have its effect mediated by the resulting disruption of the child's home life. We chose a statistical technique which could estimate both the direct and the mediated effects, i.e., Jöreskog's (1972) maximum likelihood estimation procedure for structural equations (LISREL). LISREL is a special case of Jöreskog's earlier analysis of co-variance structures (Jöreskog, 1970) and is an advanced form of path analysis. It is a statistical tool which has great advantages for the analysis of data from longitudinal projects.

**Definition of constructs.** In the Jöreskog LISREL path analysis important factors are represented as constructs. The constructs are not directly measured, but are defined by indicators. These indicators of a construct go through a process which may be seen as roughly analogous to the development of communalities in factor analysis.
These "commonalities" then represent the construct. Rather than relate the individual, and relatively unreliable, indicators to one another; the constructs are interrelated. This serves to reduce some of the lack of reliability inherent in any individual indicator of a construct. For example, as indicators of the construct "separation from parents" (separation) in the first five years of life, we used three indicators from the first five years of life: 1) amount of separation from the father, 2) amount of separation from the mother, and 3) amount of time the child spent in children's homes. For the construct "age of onset of mother's schizophrenia" (mother's onset) we used two indicators: 1) age of first appearance of symptoms, 2) age at first psychiatric hospitalization. Thus, when we are interrelating separation and mother's onset we are interrelating two construct rather than individual indicators.

The indicators of the constructs. Table 7 lists the constructs and their indicators. Certain of the constructs may require explanation.

Insert Table 7 about here

Age of onset of mother's schizophrenia (mother's onset). Age of onset of schizophrenia is a rather good indicator of the seriousness of the condition. The mother's age at the beginning of symptoms was taken from her hospital case
record. Her age at first hospital admission was taken from the Risskov Demographic Institute's Psychiatric Register.

Pregnancy and birth complications (PBCs). The scale has been described in previous publications (Mednick, 1970; Mirdal, et al, 1974). It is based on weights assigned by obstetricians and pediatricians to the various pregnancy and delivery complications noted by Danish midwives in their reports.

ANS (recovery x responsiveness). In the above discussions of the theory we have indicated that if an individual is relatively autonically unresponsive, fast recovery will be that much less of an aptitude for avoidance learning. Conversely, a highly sensitive ANS will not lead to schizophrenia if not associated with fast recovery. Thus, the theory specifies an interaction effect which can be most simply expressed mathematically, in a single score, as a product of recovery rate and responsiveness. "Responsiveness" was taken as the percent of measurable responses in the entire 1962 electrodermal examination. Mean recovery rates were taken from conditioning, tests for conditioning and extinction testing. The distribution of recovery rates in the high-risk group evidenced kurtosis. This was due to a small group of the most schizophrenic high-risk subjects who had the very fastest recovery rates. These outliers (who will be the subject of special study) resulted in highly exaggerated correlations between recovery rate...
and the outcome variables (such as hallucinations and delusions). Before producing the recovery-responsiveness products we transformed the recovery rates by a square root transformation which reduced kurtosis to an acceptable level. The intercorrelations of recovery rates and the three product scores were .90, .86 and .92; the intercorrelations of the percent responses with the three product scores were .73, .70, .68.

Schizophrenia in the high-risk children. The diagnostic interview took about three-and-one-quarter hours and consisted of a rather extensive series of symptom descriptor items. These items were subjected to factor analyses which yielded (among others) four factors which described the schizophrenia symptoms of the high-risk children (see Table 8). The four factors were named 1) hallucinations and delusions, 2) "hebephrenic" features, 3) thought disorder, and 4) autistic features.

Results of path analysis

We shall express the results of the path analysis in two ways. First by means of path diagrams we shall present the significant direct effects, then by means of bar
graphs we shall consider the sum of the direct and indirect effects of the hypothesized predispositional variables on the outcome, schizophrenia.

Path diagrams. Figure 1 presents the path diagram for men. Significant path coefficients (and their probability levels) are indicated. Note that "PBC's have no direct effect on "schizophrenia; its effect is mediated by the ANS construct. Childhood separation and the ANS construct are directly related to later schizophrenia in high-risk men, as hypothesized. Also as hypothesized, the ANS factors are rather well predicted by PBCs. Childhood separation is predicted by an early age of onset of the mother's schizophrenia which does not evidence a direct relation to schizophrenia.

The LISREL computer program calculates a multiple r of .62 for the prediction of schizophrenia by these predispositional variables for the high-risk men.

Figure 2 presents the path diagram for the women. In this path diagram the only construct which is significantly directly related to the development of schizophrenia is the age of onset of the mother's schizophrenia. The pat-
tern for the women is quite different from that seen in Figure 1 for men. The ANS construct (a reliable predictor for men) is not significantly related to schizophrenia in women, nor is childhood separation. Comparison of the path diagrams strongly suggests that some aspects of the etiology of schizophrenia are quite different in high-risk men and women. The multiple \( r \) for the prediction of schizophrenia for women is .49.

**Direct and indirect effects.** Before leaving the path diagrams, note that in these reported relationships social economic status (SES) is included and consequently held constant. SES has no direct, significant relationship with the construct schizophrenia. It does, however, influence schizophrenia via the mother’s age of onset (in men and women) and amount of childhood separation (in the case of the men). The indirect effect of SES on schizophrenia via separation may be calculated by simply multiplying the two relevant path coefficients (.26 x .40), yielding an indirect effect of .104. Note that we have earlier observed a similar interaction of social class and separation experience in relation to breakdown (Stern, et al, 1974).

By adding the direct and indirect effects onto schizophrenia, the total effect of each construct in this path
Diagram can be calculated. Figure 3 presents a bar graph depicting the total direct and indirect effects of each of the constructs on the construct schizophrenia.

**Discussion of path analysis results**

From the lives of our high-risk subject we have chosen a small group of childhood variables to explore their relationship to the subject's current diagnosis of schizophrenia. These early factors seem to relate to the development of schizophrenia quite differently for men and women.

In interpreting these results we must keep in mind the fact that for women, schizophrenia tends to have a later onset (greater incidence for women of the age of 35, Yolles and Kramer, 1969). This assessment took place when the subjects ranged from 20-30 years of age; the results for the later-onset women may be different.

Aside from this age factor we cannot suggest other serious reservations regarding these findings. Perhaps, in some cases, the 1972 interviewer learned about the separation factor (and even something about the mother's age...
of onset) while talking to the subjects. It seems rather unlikely, however, that this would affect her coding of the schizophrenia symptoms listed in Table 7. It seems even more unlikely that her ratings would be influenced differently for men and women. At the time of the interview (and in fact to date) the interviewer was totally blind regarding the perinatal and psychophysiological data. It should perhaps also be pointed out that at the time these early variables were recorded, there was no information available regarding who, among the high-risk subjects, would become schizophrenic.

It does not seem overly imprudent to begin to accept the possibility that these four factors have some relationship to the development of schizophrenia in these high-risk individuals. The interpretation of the meaning of these results, some of which were rather unexpected, may be less straightforward.

Early detection

Our initial aim is the identification of factors which might be useful in the early detection of individuals in the general population who are at high risk for schizophrenia. With respect to this aim, these four early factors are worthy of some consideration and testing. However, it should be pointed out that we have only demonstrated that they predict reliably within a group of children born to
schizophrenic women. The level of separation from the parents experienced by these children is unusually high. In a general population, this factor may not account for as high a proportion of the variance as it does for these high-risk families. The variable, age of onset of the mother's schizophrenia, is also not generally and directly applicable to population studies. Perhaps when we understand better what role mother's early onset plays in their daughter's schizophrenia, some hypotheses regarding predictive measures may be suggested.

The ANS construct (the product of recovery and responsiveness) is an individual measure which is more promising for utilization in early detection in general populations. It has been a central variable in the theoretical framework of our research for the past 20 years. It predicted quite well the 1967 psychiatric breakdowns; almost all published studies with schizophrenics (with one exception, Maricq and Edelberg, 1975) have supported the hypothesis of faster ANS recovery for schizophrenics (see Mednick, in press; Mednick, et al, 1975). Interestingly enough, almost all of these studies have been carried out on male schizophrenics. Our path analysis suggests that these reported results would not replicate with female schizophrenics. One of us, in informal attempts, (P.H.V.) has repeatedly failed to find ANS differences between female controls and female schizophrenics. The ANS measures would seem to be a useful addition to an assessment of risk.
in a male general population.

These ANS results also support our reliance on fast ANS recovery and responsiveness for selection of the high-risk three-year olds in Mauritius. These sex-specific ANS results will now send us back to our Mauritius data to attempt to find analogous relationships.

Interpretation of findings

It is the fate of longitudinal researchers to continually be presenting interim results. Now we must await the next wave of schizophrenic breakdowns as we have indicated above. In addition to these inexorable developments and changes in our subjects over the years, we also face the problem of analysing literally lifetimes of data. In our case we are slowly and more or less systematically (but certainly slowly) analysing the individual and life-event factors related to the outcome, schizophrenia. This is an analysis which is very much in progress. Thus, this report must be understood as interim also for this reason. We now will attempt to transmit to you our reflections on the meaning of these results. These reflections will suggest our strategy for future data analyses. We present these reflections very tentatively for each of the early factors which were shown to relate to the construct, schizophrenia.
Mother's age of onset: Figure 3 depicts the direct and indirect effects of mother's age of onset on the construct of schizophrenia for both men and women. Note that while there is a strong tendency for "onset" to relate to schizophrenia in the males, the relationship is almost completely mediated by "separation". Sons of "early-onset" women have an especially heightened risk of themselves becoming schizophrenic. This relationship seems to be almost completely explained by the separation from parents which follows the mother's early onset of illness.

In the women, the "onset" variable also has an important relationship to later schizophrenia. However, in the case of the women the indirect effects are negligible. This simply means that either the effect is actually only direct, or that the critical mediators were not included in this path analysis. We examined correlation matrices including some early childhood variables and "onset" for the male and female high-risk children. Early onset of the mother's illness is associated mildly and significantly with the girls evidencing low verbal IQ, disturbed and peculiar word associations and continual associations, and adult thought disorder. Curiously enough, in males none of these relationships are observed. For the males,
mother's early onset is better related to adult characteristics associated with a diagnosis of "psychopathy".

Some tentative reflections

1. Perhaps the seriously ill mother is genetically transferring some language deviation to their daughters and not to their sons. This sex-linked transmission is, of course, a possibility which we must contrast with an identification-learning hypothesis. We must relate the seriousness of the daughter's illness to the amount of contact she had with her mother. The course of illness for the HR parents and their children is currently being compared in a doctoral dissertation by Ms. Shelley Kramer-Dover.

2. The earlier development of language behavior in girls than in boys, and the fact that girls tend more to identify with their mothers may combine to differentially influence the associative and verbal responses of daughters of severely schizophrenic women. Maccoby and Jacklin (1974) suggest that this childhood advantage of girls in the acquisition of language behavior probably exists only before the age of three. In future analyses this suggestion may help us to pinpoint possible critical periods of development for further intensive analysis. Careful analysis of our case files should enable us to estimate the amount and closeness of the contact between the mothers and their
children at various age levels as well as the relation between the child's age at the time of mother's breakdown and the child's adult diagnostic status.

3. It is also possible that the more seriously schizophrenic mothers pass on some specific characteristic to both their daughters and their sons. But perhaps this characteristic predisposes to schizophrenia only in the daughter because of differences in the manner in which society deals with the two sexes. We shall return to this thought when we discuss the ANS construct.

4. In male, high-risk children, "onset" is not directly related to schizophrenia. As mentioned, inspection of the case material for the boys indicates that for them, "mother's early-onset" is significantly associated with adult symptoms of psychopathy. We know that the schizophrenic mothers (in this sample) tend to mate with criminal men (Kirkegaard-Sorensen and Mednick, 1976; see also Lewis, 1976). We intend to examine the possibility that for the most early-onset schizophrenic women this tendency is even stronger. If this is true, it might explain the heightened psychopathy of the sons who have early-onset mothers (Schulsinger, 1972; Hutchings and Mednick, 1974). It might also suggest hypotheses regarding the mother-daughter findings.

Separation in childhood (0-5 years). Early separation
from parents is highly and significantly related to later schizophrenia for male, but not for female, high-risk children. The path coefficient for the females is in the same direction as for the males, but not statistically significant. Differences between the girls and boys in amount of separation are minimal and not statistically significant.

1. The amount of separation experienced by the boys (but not the girls) is related negatively to their social class status. It is possible this social class factor may mean that the treatment of boys separated from their parents is of a different (poorer) quality than than the treatment of girls. We shall attempt some modest examination of this possibility by interviewing individuals who worked in these children's homes in the 40's and 50's. We must also check to see whether reasons for selection of children to be placed in children's homes are different for the two sexes. We do have some suggestive evidence, for a subsample of the HR group, that children's home placement is partly dependent on pre-placement infant characteristics (Herrmann, 1973).

2. Perhaps the reason early separation is a more important variable for boys than girls is that boys experience more "separation anxiety". While the research evidence on this issue is far from unequivocal, Maccoby and Jacklin (1974) suggest that where sex differences exist "boys cry more when the mother or father leaves the room; and at the
early age of 9-10 months they are more likely to crawl quickly after the mother if she moves into an adjacent room" (page 196). Perhaps the boys in this study (because of their sex-linked immaturity) did suffer a stronger separation reaction than did the girls. This may have, in some way, been involved in the chain of events leading to their eventual schizophrenia. Unfortunately, our longitudinal project does not contain reliable data concerning the children's reactions to their separation from their parents. The high ANS reactivity of the boys who eventually became schizophrenic could suggest that separation from their parents may have produced a relatively strong emotional reaction.

PBC factors. The high-risk boys suffered slightly more serious and a greater number of perinatal complications than the girls (not statistically significant). This direction of results is in keeping with our expectations. For boys there is a large significant relationship between PBC and later schizophrenia (Figure 3). The relationship for the girls is actually negative (not statistically significant). For the boys, most of the PBC-schizophrenia relationship is mediated by ANS-schizophrenic relationship which is not found in the girls.

There is evidence that females' electrodermal responsiveness is related to their menstrual cycle (Bell, et al, 1975). One could suggest the hypothesis that the lack of
a relationship between ANS factors and schizophrenia for the females is due to a menstrual cycle-related lack of reliability of the ANS measures in the females. (We failed to note menstrual data in 1962.) Note, however, that the PBC-ANS relationship is at least as strong in the females as it is in the males. It is unlikely that this would be true, unless the females' ANS responsiveness was as reliable as the males' ANS reactivity and recovery are reliably related to PBCs in the girls, but this increased reactivity is not associated with an increased risk of schizophrenia.

"ANS factors. We have observed unexpected sex difference in the effect of the ANS factor on schizophrenia. These differences are puzzling; we offer some observations related to sex-differences in ANS-relevant emotional behavior.

What are the nature of sex-differences-related emotional reactivity?

Maccoby and Jacklin (1974) suggest that if there are sex differences in amount of emotionality, they are very small. The self-reported lower fearfulness of boys is almost certainly explained by their unwillingness to admit their fears and anxieties. Boys are much more defensive than girls. For a boy to admit emotionality, is to admit a weakness and to risk being called a "sissy". Girls "are
simply more willing than boys to admit that they feel anxious" (Maccoby and Jacklin, 1974, page 186). It is not unfeminine to admit being afraid. Boys conceal and avoid such emotions more than girls do. Under some conditions and in some social circumstances, emotionality in women may be seen as a positive, feminine attribute. In males it is often regarded with considerable suspicion; it is not masculine.

Little girls are freer to express fear and to cry when disappointed without being judged a sex-role deviant. "Parents show considerable more concern over a boy being a "sissy" than over a girl being a tomboy" (Maccoby and Jacklin, 1974, page 362). Perhaps girls have less need than boys to avoid expressing fear or anxiety. In that case perhaps little girls need not learn deviant ways of thinking and behaving to avoid emotional expression.

Little boys tend to learn that they must avoid emotional expression. The little boy who has an extremely reactive ANS may often be pushed by parents, guardians, teachers, and peers to suppress this emotionality. Thus, any response (such as irrelevant thought or bizarre behavior) which will avoid an encounter with a potentially emotion-provoking stimulus (such as an approaching person) will be reinforced and quickly learned. Fast ANS recovery will assure a relatively powerful reinforcement for such an avoidance response and will increase its probability.
of being elicited. The repetition of this learning sequence over the years could produce an effective screen of avoidance behavior which will function to isolate the schizophrenic and support his withdrawal. What about the female schizophrenics? This discussion implies that (not being influenced by the ANS factors) the women should develop a less withdrawn form of schizophrenia. The clinical picture for the male schizophrenics is dominated by withdrawal, isolation, thought disorder, and hallucinations. The women evidence serious thought disorder, but are frequently quite promiscuous and socially "active". The fact that schizophrenic women become married three times as often as schizophrenic men (Forrest and Hay, 1972) probably has many explanations, but in any case does testify to less avoidant, withdrawn behavior than is the case for male schizophrenics. Forrest and Hay (1972) express some suspicion regarding early onset diagnoses of schizophrenia in women. They report that it has been their experience (over a specific two year period) that "almost every female patient first admitted under the age of 20 years with a presumptive diagnosis of schizophrenia later has this diagnosis revised to personality disorder or manic-depressive illness" (page 55). This statement is probably too extreme for most clinicians to accept.

These reflections suggest two related notions which may repay some consideration by investigators. First, perhaps the condition we call schizophrenia takes a different
form in men and women; second, perhaps the etiology is, in part, different for men and women.

Most investigators (including ourselves) have until now neglected to consider the possibility of sex differences in the schizophrenics. Frequently, an area of research which has almost exclusively studied male schizophrenics is reviewed (with no mention of the sex variable) and the conclusions generalized to all schizophrenics. These analyses suggest that we may explain more variance if we consider the sexes separately.

**Conclusions**

The presence of schizophrenia in HR women is related negatively to the age of onset of their mothers' illness. The factors of early parental separation, ANS recovery and responsiveness and perinatal complications did not relate significantly to the development of schizophrenia in these HR women.

In men the pattern is quite different. The age of onset of the mother's illness is related to schizophrenia in her son only because it produces parental separation. Parental separation relates directly to the development of schizophrenia in the HR boys. Perinatal complications in male HR children relate to their later development of schizophrenia. This apparently results in large part be-
cause the perinatal complications seem to produce ANS-
fast recovery-responsiveness effects in the HR children.
In the HR boys the ANS deviance is reliably related to the
later development of schizophrenia.

The discussion suggests that the form which schizo-
phrenia takes in men and women may be different along the
withdrawal-activity dimension (Depue, 1976; Plovnick, 1976).
These differences may be related to the hypothesized role
of ANS factors in the learning of avoidance-withdrawal.
Footnotes

1 The high-risk research is being supported by USPHS Grant No. MH 25325 and was supported earlier by the Foundation for Child Development. The perinatal study was supported by MH 19225. The Mauritius research was originally supported by grants to the Psykologisk Institut from the World Health Organization. We wish to express our gratitude to the Mauritian government for their continuing support during the entire project and to date. The assessment of the Mauritian children was supported by a grant from the British Medical Research Council to Venables. The Danish Organization for Aid to Developing Nations (DANIDA) supported the nursery schools.

2 For those familiar with the 1962 Copenhagen high-risk project and its theoretical basis, it might be less boring for them if they proceed directly to page 11 or 14.

3 We wish to thank the test authors for their helpful co-operation in this work.

4 We wish to thank Drs. Lise Hauge and R. Rosenberg for their work on the reliability tests.

5 This analogy is presented for heuristic purposes only. The actual process is not mathematically related to factor analysis.
Of the interviewer's 13 schizophrenics, six were female and seven were male.
References


Kirkegaard-Sørensen, L., and Mednick, S.A. Registered criminality in families with children at high risk for schizophrenia. *Journal of Abnormal Psychology*, 1975, 84, 197-204.


Mednick, S.A. A learning theory approach to research in schizophrenia. Psychological Bulletin, 1958, 55, 316-327.


Mirdal, G., Mednick, S.A., Schulsinger, F., and Fuchs, F.


Plovnick, N. Autonomic nervous system functioning as a predisposing influence on personality, psychopathy and schizophrenia. Doctoral dissertation, Graduate Faculty, New School for Social Research, 1976.


Table 1

CHARACTERISTICS OF THE EXPERIMENTAL AND CONTROL SAMPLES

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control</th>
<th>Experimental</th>
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</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>104</td>
<td>207</td>
</tr>
<tr>
<td>Number of boys</td>
<td>59</td>
<td>121</td>
</tr>
<tr>
<td>Number of girls</td>
<td>45</td>
<td>86</td>
</tr>
<tr>
<td>Mean age*</td>
<td>15.1</td>
<td>15.1</td>
</tr>
<tr>
<td>Mean social class**</td>
<td>2.3</td>
<td>2.2</td>
</tr>
<tr>
<td>Mean years education</td>
<td>7.3</td>
<td>7.0</td>
</tr>
<tr>
<td>Per cent of group in children's homes (5 years or more)+</td>
<td>14 %</td>
<td>16 %</td>
</tr>
<tr>
<td>Mean number of years in children's homes (5 years or more)+</td>
<td>8.5</td>
<td>9.4</td>
</tr>
<tr>
<td>Per cent of group with rural residence++</td>
<td>22 %</td>
<td>26 %</td>
</tr>
</tbody>
</table>

*Defined as age to the nearest whole year.

**The scale runs from 0 (low) to 6 (high) and was adapted from Svalastoga (1959).

†We only considered experience in children's homes of 5 years or greater duration. Many of the Experimental children had been to children's homes for brief periods while their mothers were hospitalized. These experiences were seen as quite different from the experience of children who actually had to make a children's home their home until they could go out and earn their own living.

++A rural residence was defined as living in a town with a population of 2500 persons or fewer.
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TABLE 3

DESCRIPTIONS OF CONDITIONS OF SICK GROUP

Male, born 16 March 1953; extremely withdrawn, no close contacts, 2 months' psychiatric admission following theft, currently in institution for boys with behavior difficulties, still performing petty thievery.

Female, born 19 January 1943; married, one child, extremely withdrawn, nervous. Evidence of delusional thinking, pulls her hair out, has large bald area.

Female, born 27 March 1946; promiscuous, highly unstable in work, no close contacts, confused and unrealistic, psychiatric admission for diagnostic reasons, recent abortion, some evidence of thought disorder.

Male, born 1 July 1946; under minor provocation had had semipsychotic breakdown in Army, expresses strange distortions of his body image, thought processes vague, immature.

Male, born 2 May 1944; severe difficulties in concentrating; cannot complete tasks; marked schizoid character; marginally adjusted.

Male, born 3 June 1947; lonely in the extreme; spends all spare time at home; manages at home only by virtue of extremely compulsive routines; no heterosexual activity; marked schizoid character.

Male born 1 October 1953; no close contact with peers, attends class for retarded children, abuses younger children, recently took a little boy out in the forest, undressed him, urinated on him and his clothes, and sent him home.

Male, born 17 January 1954; has history of convulsion, constantly takes anti-seizure drug (Dilanthin), nervous, confabulating, unhappy, sees frightening "nightmares" during the day; afraid of going to sleep because of nightmares and fear that people are watching through the window, feels teacher punishes him unjustly.

Female, born 18 March 1944; nervous quick mood changes; body image distortions, passive, resigned; psychiatric admission, paranoid tendencies revealed, vague train of thought.
Male, born 14 March 1952; arrested for involvement in theft of motorbike; extremely withdrawn, difficulties in concentration; passive, disinterested, father objected to his being institutionalized; consequently he is now out under psychiatric supervision.

Male, born 19 October 1947; level of intellectual performance in apprenticeship decreasing; private life extremely disorderly; abreacts through alcoholism.

Male, born 20 January 1944; severe schizoid character, no heterosexual activity; lives an immature, shy, anhedonic life, thought disturbances revealed in TAT.

Female, born 25 May 1947; psychiatric admission, abortion, hospital report suspects pseudoneurotic or early schizophrenia; association tests betray thought disturbance, tense, guarded, ambivalent. Current difficulties somewhat precipitated by sudden death of boy friend.

Male, born 13 August 1950; sensitive, negativistic, unrealistic; recently stopped working and was referred to a youth guidance clinic for evaluation. Is now under regular supervision of a psychologist.

Male, born 28 January 1953; perhaps borderline retarded; psychiatric admission for diagnostic reasons; spells of uncontrolled behavior.

Male, born 23 June 1958; repeatedly apprehended for stealing; severe mood swings, sensitive, restless, unrealistic; fired from job because of financial irregularities.
Female, born 5 July 1941; highly intelligent girl with mystical interests. Very much afflicted by mother's schizophrenia. TAT reveals thought disorder. Receiving psychotherapy.
Table 4

Distinguishing characteristics of the Sick Group

1. Lest mother to psychiatric hospitalization relatively early in life.
2. Teacher reports disturbing, aggressive behavior in school.
3. Evidence of associative drift.
4. Psychophysiological anomalies.
   A. Markedly fast latency of response.
   B. Response latency evidence no signs of habituation.
   C. Resistance to experimental extinction of conditioned GSR.
   D. Remarkably fast rate of recovery following response peak.
5. 70% of the Sick Group had suffered serious pregnancy and/or birth complications.
<table>
<thead>
<tr>
<th></th>
<th>High Risk (N = 207)</th>
<th>Low Risk (N = 104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full assessment complete</td>
<td>173</td>
<td>91</td>
</tr>
<tr>
<td>Home interview only (social worker)</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Not yet contacted* (Parent objected or the subject could not be located)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Living abroad*</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Deceased</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Subject refused</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

*Table 5*
### Table 6

**IDENTIFYING CHARACTERISTICS OF HIGH AND LOW RISK SUBJECTS PARTICIPATING IN FULL INTERVIEW (1972)**

<table>
<thead>
<tr>
<th></th>
<th>High Risk</th>
<th>Low Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number - full interview</td>
<td>173</td>
<td>91</td>
</tr>
<tr>
<td>Mean age at 1962 assessment</td>
<td>14.9</td>
<td>15.1</td>
</tr>
<tr>
<td>Mean social class</td>
<td>2.1</td>
<td>2.4</td>
</tr>
<tr>
<td>Number males</td>
<td>97</td>
<td>53</td>
</tr>
<tr>
<td>Number females</td>
<td>76</td>
<td>38</td>
</tr>
</tbody>
</table>

---

**Note:** The numbers in parentheses indicate the number of subjects in the initial interview and the number of subjects in the follow-up interview. For example, 97 (24) indicates 97 subjects were interviewed initially and 24 of those were followed up.
FIGURE 1
PATH DIAGRAM FOR MEN

MULTIPLE R = .62

MOTHER'S AGE OF ONSET

SOCIAL CLASS

PREGNANCY, BIRTH COMPLICATIONS

PARENTAL SEPARATION

AUTONOMIC NERVOUS SYSTEM

AVERAGE AGE OF SAMPLE IN YEARS

.50 -- PATH COEFFICIENT
(.01) -- SIGNIFICANCE LEVEL

.36 (.001)

.40 (.01)

.32 (.

.26 (.02)

-.49 (.0001)

PAGE 59
Figure 2
Path Diagram for Women

- Mother's Age of Onset
- Social Class
- Prenatal Complication
- Autonomic Nervous System
- Schizophrenia

Path Coefficient

.50 -- Path Coefficient
.01 -- Significance Level

Average Age of Sample in Years

0 5 10 15 20 25
DIRECT AND INDIRECT EFFECTS OF CHILDHOOD CONSTRUCTS ON SCHIZOPHRENIA CONSTRUCT

**Figure 3**

Mother's Age of Onset | Separation | PBC | ANS

Path Coefficients

Indirect Effects

Direct Effects

Female | Males