

## Perinatal Complications and Clinical Outcome within the Schizophrenia Spectrum

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**Summary:** In a prospective study of offspring of schizophrenic mothers, perinatal complications reported in midwife protocols were analysed for those offspring who, as adults, were diagnosed as schizophrenic, borderline schizophrenic or as not suffering from mental illness. The schizophrenics were found to have had the most complicated births, and the borderlines, the least complicated births. This difference is interpreted in terms of a 'diathesis-stress' model. It is proposed that birth complications can decompensate borderline individuals towards schizophrenic breakdown.

In the search for aetiological factors in schizophrenia, attention has frequently been focused upon the putative role of *pregnancy and birth complications* (PBCs). These can be defined as deviations from an expected course of events during pregnancy, labour, delivery and early neonatal period prior to discharge from the obstetric ward. There is increasing evidence, reviewed by McNeil and Kaij (1978), that schizophrenics have frequently suffered PBCs. This evidence derives from three principal sources: retrospective studies of hospitalized schizophrenics, studies of monozygotic twins discordant for schizophrenia, and studies of the offspring of schizophrenics. McNeil and Kaij conclude that "obstetric complications seem to interact with genetic influence towards schizophrenia and that such complications, occurring prior to schizophrenia in the offspring, are independent, stressful factors and not a manifestation of 'schizophrenic' genes".

The present investigation reports findings obtained from an on-going longitudinal, prospective study of offspring of severely schizophrenic mothers (Mednick and Schulsinger, 1965). This High Risk Study has to date yielded several results bearing upon the role of PBCs in schizophrenia. It has previously been reported that high-risk individuals as a group had not experienced more PBCs than a matched low-risk control group (Mirdal *et al*, 1974), i.e. that reproduction by schizophrenic women is not accompanied by an elevated frequency of PBCs. However, Mednick (1970) demonstrated PBCs to have occurred more frequently among those high-risk individuals who had suffered some form of psychiatric breakdown, not necessarily schizophrenia, by the time of the first

follow-up in 1967, at which time the mean age of the high-risk sample was 20 years. Mednick *et al* (1978) observed a positive correlation between PBCs and delusions and hallucinations for male subjects. This correlation appeared to be mediated by the lability of the autonomic nervous system, as measured by electrodermal activity.

The present investigation examines the relationship of PBCs to the specific diagnoses of schizophrenia and of borderline schizophrenia among the high-risk individuals. The concept of borderline schizophrenia utilized here corresponds to the Diagnostic and Statistical Manual of Mental Disorders (DSM) III (1980) diagnosis schizotypal personality disorder. Our interest in the diagnosis of borderline schizophrenia arises from the theoretical position that this disorder can be regarded as a more fortunate outcome of a genotype comparable to that with which schizophrenics are disadvantaged. A genetic link between these two disorders has been demonstrated in adoptive studies (Kety *et al*, 1978), and, in fact, the DSM concept of schizotypal personality has been partly developed on the basis of these studies (Spitzer and Endicott, 1979). The psychopathological picture of borderline schizophrenia may be viewed as a dilute form of schizophrenia, i.e. essentially characterized by the subtle presence of fundamental schizophrenic symptoms (Bleuler, 1961) such as formal thought disorder and disturbed emotional contact, and a relatively intact reality testing reflected by lesser intensity and duration of accessory symptoms such as delusions and hallucinations. We have demonstrated (Parnas *et al*, accepted for publication) that at *premorbid assessment* of the high-risk group, schizophrenics exhibited more

difficulty in affective control and displayed poorer attention than did borderline schizophrenics. We have suggested that this difference might be an expression of a subtle neurological deficit among the schizophrenics, a deficit which itself could have resulted from PBCs.

### Samples and Methods

In 1962 Mednick and Schulsinger (1965) began a prospective study of 207 children of severely schizophrenic mothers. The mean age of the sample in 1962 was 15.1 years.

In addition to the various psychological, psychophysiological and social measures that were recorded in 1962, the children's birth records were also obtained. Virtually all births in Denmark are attended by a midwife who completes a standardized form concerning the course of the delivery as well as the pre- and postnatal condition of both the mother and the newborn. The midwife protocols of 166 of the 207 High Risk subjects were located and transcribed.

In addition to examining the frequencies of specific obstetric complications, the presence or absence of

which is reported in the midwife protocol, we also utilized three different global scores of PBCs:

1. *Frequency score* indicating the number of distinct PBCs reported, regardless of their severity.
2. *Severity score* representing the weight of the single most severe complication experienced by the newborn. This weighting system was developed in collaboration with Professor Fritz Fuchs of the Department of Obstetrics and Gynaecology, Cornell University. The system is shown in Table I.
3. *Total score* derived by adding all the individual weighted scores. As an example, a child born (a) with the umbilical cord around its neck (severity score 4), and (b) after 48 hours of labour, severity score 3) and (c) with the use of forceps (severity score 1), would receive a Frequency Score of 3, a Severity Score of 4, and a Total Score of 8.

A ten year follow-up was undertaken in 1972-1974 (Schulsinger, 1976) consisting of, amongst other test procedures, a thorough diagnostic assessment. This assessment, lasting approximately four hours, comprised Current and Past Psychopathology Scale (CAPPS) (Endicott and Spitzer, 1972), Present State Examination (PSE) (Wing *et al*, 1974), and additional scales for thought disorder, ego-organization, personality traits, and pseudoneurotic or pseudopsychopathic characteristics.

On the basis of this assessment the interviewer (H.S.) made a clinical diagnosis according to WHO (1967) criteria. The following groups from the clinical diagnosis were selected for the present comparison.

1. *Schizophrenia*: The interviewer's diagnosis of schizophrenia was based on the presence of Bleuler's (1961) fundamental symptoms (thought disorder, autism, ambivalence, emotional blunting) as well as his accessory symptoms (delusions and hallucinations). For a diagnosis of schizophrenia it was not necessary that all of these symptoms be observed at the time of the interview; they might also be drawn from the anamnesis. However, thought disorder, autism, and emotional blunting were required for a schizophrenia diagnosis. Birth records were available for 12 (7 males) of the 13 individuals who received this diagnosis.
2. *Borderline schizophrenia*: This diagnosis was made on the presence of subtle formal thought disorder, narcissistic contact, pan-neurosis, pan-anxiety, fluctuating neurotic symptoms, micropsychotic episodes (Hoch and Polatin, 1949), and, in the case of pseudopsychopathic

TABLE I

*Severity weight allocations for specific complications*

Weights	
0	= No complications
1	= Forceps used Caesarean section Placental defects Previous foetal loss Bleeding after delivery Adipositas Narrow pelvis Mother's illness during pregnancy Twins Labour time above 24 hours
2	= Mother's serious illnesses Infarcts in the placenta Bad foetal position Premature rupture of membranes Contractions of pelvis during delivery Primary uterine inertia Signs of prematurity with weight above 2500 grams Labour time above 36 hours
3	= Secondary uterine inertia Bleeding during delivery Labour time above 48 hours
4	= Asphyxiation Umbilical cord complications Eclampsia Signs of prematurity with weight less than 2500 grams

conditions, acting-out behaviour (Dunaif and Hoch, 1955). Birth records were available on 25 (14 males) of the 29 individuals who received this diagnosis.

3. *No mental illness*: This group included individuals diagnosed as not suffering from any mental disorder, or as suffering only from slight character neurosis. Birth records were obtained for 39 (21 males) of the 55 subjects who received the diagnosis of No Mental Illness.

For all evaluations, non-parametric two-tailed statistical methods were employed. For analyses of

specific complications, Fisher's Exact Probability Test was used. The scale scores, being ordinal in nature, were analysed with Mann-Whitney's U Tests.

### Results

The distribution of specific complications for each of the three diagnostic groups is shown in Table II. Considered separately in this way, the only significant difference concerned bad foetal position which occurred more frequently among schizophrenics than among both borderlines and no mental illness individuals. Notwithstanding the lack of other

TABLE II  
*Observed complications*

	Schizophrenia		Borderline schizophrenia		No mental illness	
	N	%	N	%	N	%
Eclampsia	0	(0)	0	(0)	1	(2.5)
Previous foetal loss	0	(0)	0	(0)	1	(2.5)
Premature rupture of membranes	1	(8.3)	1	(4)	9	(23)
Abnormal foetal position*	3	(25)	0	(0)	0	(0)
Narrow pelvis	0	(0)	0	(0)	1	(2.5)
Pelvic contractions during delivery	1	(8.3)	0	(0)	1	(2.5)
Bleeding during delivery	0	(0)	1	(4)	1	(2.5)
Bleeding after delivery	1	(8.3)	1	(4)	0	(0)
Asphyxia	1	(8.3)	0	(0)	2	(5.1)
Umbilical cord complications	2	(16.6)	0	(0)	1	(2.5)
Primary uterine inertia	0	(0)	0	(0)	1	(2.5)
Secondary uterine inertia	1	(8.3)	0	(0)	1	(2.5)
Forceps used	2	(16.6)	0	(0)	1	(2.5)
Caesarean section	0	(0)	0	(0)	1	(2.5)
Signs of prematurity > 2500 g	2	(16.6)	1	(4)	2	(5.1)
Signs of prematurity < 2500 g	0	(0)	1	(4)	3	(7.7)
Placental abnormalities	1	(8.3)	2	(8)	1	(2.5)
Labour > 24 hours	2	(16.6)	2	(8)	3	(7.7)
Labour > 48 hours	1	(8.3)	1	(4)	3	(7.7)

\* Frequency among schizophrenics is higher than both among borderlines ( $P = 0.028$ ) and no mental illness individuals ( $P = 0.011$ ).

TABLE III  
*Mean scale scores in the three diagnostic groups*

	Schizophrenia		Borderline schizophrenia		No mental illness		Mann Whitney's U-test P value Schizophrenia vs borderline
	Mean	SD	Mean	SD	Mean	SD	
PBC frequency score	1.50	1.38	0.40	0.76	0.85	1.09	0.009
PBC severity score	1.08	0.90	0.40	0.71	0.72	0.83	0.019
PBC total score	3.17	2.82	0.76	1.67	1.92	2.85	0.008

significant differences in these individual complications, a general trend towards more complications among the schizophrenics and fewer among the borderlines, relative to the no mental illness group, can be discerned.

This trend becomes more clearly manifest in the three scales scores—namely Frequency, Severity, and Total Scores. Statistical comparisons (Table III) have confirmed that on all three scales, the schizophrenic group has significantly higher complication scores than the borderline group. The mean values for the no mental illness group do not differ significantly from either those of the schizophrenics or those of the borderlines. In fact, the mean values for the no mental illness group lie close to the midpoint between these two pathological groups. The majority of schizophrenics (67 per cent) experienced some or other form of complication, i.e. it was not the case that all of the complications observed within the schizophrenic group were concentrated upon only a few of their number.

Although the other, non-schizophrenia spectrum diagnostic groups from 1972 follow up (Schulsinger, 1976) were not the object of the present study, it is worthwhile mentioning in this context, that PBC scores for the schizophrenics and for the borderlines were respectively higher and lower than for any of those other diagnostic groups. We have also explored the possibility of an interaction of sex with the PBC differences of the diagnostic groups. The number of subjects becomes too small for statistical analysis, but there is no suggestion that the sexes respond differently in diagnostic outcome to the occurrence of PBCs.

### Discussion

The interpretation of our findings necessitates consideration of some methodological issues. First, it is important to note that, at the time of the diagnostic follow-up in 1972–1974, the subjects' mean age was 24 years, with a range from 18 to 30 years. This implies that the entire sample had not passed through the risk period for schizophrenia. For this reason the results presented are provisional, in the sense that some further schizophrenic cases may evolve, some of them from the borderline group (Hoch *et al*, 1962). This may well suggest that the observed PBC distribution among schizophrenics and borderline schizophrenics is, in fact, a minimum difference.

Second, in contrast to the majority of other investigations dealing with the relationship between schizophrenia and PBCs, our study does not suffer from the potential bias of retrospective data collection, since the data were all recorded at the time of birth.

With regard to the quality of the midwife protocols, there is a consensus among Danish obstetricians, that

these protocols are conservative, in the sense that any complications reported will certainly have occurred, whereas some minor difficulties may not have been recorded.

Although we have not obtained significant differences between schizophrenics and no mental illness individuals with respect to the scale scores, there is a tendency, consistent with McNeil and Kaij's conclusion, towards more and worse complications in schizophrenics. This same tendency is to be observed in the individual complications, reaching significance in the case of abnormal foetal position.

On the other hand, the PBC scale scores among schizophrenics were found to be significantly higher than those among borderline schizophrenics. This, we feel, supports our initial hypothesis that borderline schizophrenics experience less environmental insult than do schizophrenics. This hypothesis itself derives from a broad theoretical framework, commonly termed the 'diathesis-stress model', which proposes that schizophrenia is the result of disadvantageous environmental influences acting upon a genetic predisposition (Shields, 1978). Within this framework, our present findings could be explained by assuming that both the schizophrenics and the borderlines inherited a comparable genetic loading that is more severe than that of the no mental illness group. The phenotypic outcome, i.e. whether an individual develops schizophrenia or remains borderline, would subsequently depend on the influence of environmental factors. Harmful or stressing influences would tend to produce schizophrenia in such individuals. We propose that PBCs constitute at least one important class of such influences. In order to remain borderline, the genetically predisposed individual will need to have had an exceptionally uncomplicated birth. Complications would decompensate that individual towards later schizophrenic breakdown.

Although we are not aware of any other studies specifically concerned with PBCs and borderline schizophrenia, some indirect support for our proposal may be inferred from investigations concerning the influence of organic factors upon different outcomes in schizophrenia. Pollack *et al* (1968), observed a relationship between the occurrence of early minimal brain damage (including PBCs) and poor prognosis in schizophrenia. McNeil and Kaij (1978) conclude in their survey that history of obstetric complications relates to poor outcome within schizophrenia.

Whereas a relationship between PBCs and schizophrenia seems to be well established, the apparent lack of PBCs in the birth history of borderline schizophrenics, demonstrated in this study, requires replication in other samples. If future studies confirm our findings, experimental trials may then be imple-

mented to determine whether intervention in the occurrence of PBCs in reproduction of schizophrenic parents (or samples otherwise defined as having a foetus at risk) is followed by a decrease in incidence of schizophrenia among their offspring. Such trials would permit the translation of correlational results into causative statements, on which preventive programs can be based.

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