Obstetric complications in distinct schizophrenic subgroups

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Summary – In 55 chronic DSM III-R schizophrenics the occurrence of obstetric complications (OCs) was investigated using the familial/sporadic strategy and Leonhard’s unsystematic/systematic distinction. The overall frequency and severity of OCs did not differ between patients and controls. A sub-sample of patients, whose genetic risk was supposed to be high in both classification systems (diagnosis of unsystematic and familial schizophrenia), had significantly fewer OCs than controls on the Lewis and Murray scale ($P < 0.05$). With reference to previous reports of increased mortality rates in the offspring of schizophrenics, high genetic risk and additional perinatal stressors may increase perinatal mortality. In contrast, patients whose genetic risk was supposed to be low in both systems (diagnosis of systematic and sporadic schizophrenia) showed a trend to an increased frequency of OCs in the Fuchs scale. In the context of the recently reported highly significantly increased rate of maternal infections during midgestation in these patients, it was supposed that perinatal complications may be of some aetiological importance in schizophrenics with low genetic risk.

obstetric complications / schizophrenia / familial-sporadic concept / Leonhard classification

Introduction

The influence of pregnancy and obstetric complications (OCs) on the development of schizophrenia during adulthood is a matter of on-going controversy (Goodman, 1988; Lewis, 1989). It is widely accepted that schizophrenics have significantly more prenatal and perinatal complications than their normal siblings (Woerner et al, 1973; Eagles et al, 1990). This difference persists in schizophrenics with a familial form of the disease (De Lisi et al, 1988). Furthermore, congenital risk factors seem to be more common in schizophrenia than in other psychiatric disorders (Pearlson et al, 1985; Lewis and Murray, 1987). Parnas et al (1982) reported that the offspring of schizophrenic mothers who developed schizophrenia in adulthood had a non-significant increased level of OCs than was the case for those who remained well, and those with schizotypal personality disorder had a significantly decreased level of OCs compared to the schizophrenics. As reviewed by McNeil (1991), children of schizophrenic parents, who are considered to be at increased genetic risk, do not suffer from a substantially increased rate of OCs. The author concluded that OCs are not genetically determined in reproductions among schizophrenics. There are inconsistent results regarding the question as to whether schizophrenics suffer more frequently from OCs and from more severe complications during delivery than do normal controls. Turner et al (1986) failed to find any differences between schizophrenics and age-matched controls. Jacobson and Kinney (1980) found an elevated OC level in a sample which had a mainly favourable outcome (Kety et al, 1968) as did Gillberg et al (1986) in a mixed sample of remitting “teenage psychoses”. McNeil and Kaj (1978) reported a significantly increased frequency of obstetric and neonatal complications in a sample of 54 narrowly defined “process schizophrenics”. Done’s study (1991) was based on a different type of OC scale
than that used in previous studies. This study re-
analysed data from the British perinatal mortality
survey sample taken in 1958 and found no signifi-
cantly increased level of complications associated with
perinatal death in the birth cohort in those children
who subsequently developed schizophrenia.

The concept of dividing schizophrenia into familial
(positive family history of schizophrenia) and sporadic
scizophrenia among first and/or second degree relatives) is often used in
psychiatric research (Murray and Revely, 1985). Using modern diagnostic criteria (APA, 1987), this strategy seems to be the most appro-
priate way of registering the genetic risk of the
disease (Kendler, 1987).

Another strategy dealing with the heterogeneity of schizophrenia was outlined by Karl Leonhard (1979). Continuing the work of Knaepel, Wernicke and Alzheimer, he classified schizophrenia into two
main categories on the basis of clinical symptom-
picture, course and long-term outcome. The unsys-
tematic schizophrenics with acute onset and usually
polymorphous symptomatology show a clearly
periodic course and lead to varying degrees of
residual states. In contrast, the systematic forms
lead to severe and irreversible defects in
which no marked change in symptoms is observ-
able (Franzek and Beckmann, 1992). In both
groups Leonhard subsequently found a different
heredity (Leonhard, 1979, 1980). Unsystematic
schizophrenics have a familial loading with
the homogeneous psychoses (about 20%). However, a
positive family history was mostly missing (1–3%) in
the systematic forms of schizophrenia. Therefore, if patients had a familial form and 36 a sporadic form of DSM III-R
schizophrenia.

The Leonhard classification distinguishing between
systematic and unsystematic schizophrenia
H Beckmann and E Franzek independently diagnosed all
patients according to Leonhard’s classification without
considering familial history. Unsystematic forms of schizophrenia
(mainly genetically determined according to Leonhard)
was diagnosed in 32 patients. A systematic form of schizo-
phrenia (mainly environmentally determined according to
Leonhard) was found in 23 patients.

“High genetic risk” and “low genetic risk” groups:
(genetic risk supposed to be similar in both classifi-
cation systems). Even when strong heredity is supposed, clinical manifestation of the illness may be lacking in pre-
disposed individuals simulating sporadic occurrence of the
disease in a given family. Unsystematic loading with
schizophrenic psychoses is not necessarily due to genetic
factors. This led us to form the following subgroups:

Subj ects and methods
Diagnosis in DSM III-R and Leonhard’s classification

Interviews were carried out with the mothers of 55 non-
related chronic schizophrenics (22 women, 33 men) and
20 age-matched physically and mentally healthy controls, to
investigate whether adverse events which had occurred
during the prenatal, intrapartal and postnatal periods.
Demographic and clinical characteristics of the patients
and age of their mothers at the time of interview with
regard to the various diagnostic groups were described
in detail in a previous paper in this journal (Stöber et
al., 1992). The study started on wards with chronically ill
male patients. This explains why nearly all outnumber
women in the study. Patients had to fulfill the diagnostic
criteria of chronic schizophrenia according to DSM III-
R as well as Leonhard’s group of schizophrenias. Thus,
all patients had an unfavourable outcome with severe
residual psychopathology.

Patients fulfilling Leonhard’s criteria of cycloid psy-
chooses (Leonhard, 1979), were deliberately not included,
even when DSM III-R criteria for schizophrenia were
fulfilled. After personal examination, diagnoses were
established by H Beckmann and E Franzek. Both psy-
chiatrists are experienced in both the DSM III-R and
Leonhard classification systems. In a recent study of
chronic schizophrenics, they had a coefficient of agree-
ment (Cohen’s kappa) of 0.88 within the Leonhard clas-
sification (Franzek and Beckmann, 1992).

The total sample consisted of the following groups:

<table>
<thead>
<tr>
<th>Obstructive complications</th>
<th>Controls (n = 20)</th>
<th>Total sample (n = 55)</th>
<th>DS M III-R</th>
<th>Familial</th>
<th>Sporadic (n = 19)</th>
<th>Leonhard criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>13</td>
<td>24</td>
<td>31</td>
<td>13</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Positive</td>
<td>8</td>
<td>8</td>
<td>16</td>
<td>23</td>
<td>16</td>
<td>15</td>
</tr>
</tbody>
</table>

No statistically significant differences were found. Comparisons were made using the $\chi^2$ test.

The second scale (Parnas et al., 1982) was a 25-item checklist containing a severity weighting (scored 0–4).
Each subject was assigned to three global scores: i) fre-
quency score: indicating the total number of pregnancy
and birth complications; ii) severity score: representing
the weight of the single most severe complication; iii)
total score: taking the sum of all recorded and weighted complications experienced by the subject. The scale scores were analysed using the non-parametric
Mann-Whitney-U-test and the parametric Student t-test in cases of
SQR-error.

Results

Total group of chronically schizophrenic patients

On the “obstetric and birth complication scale”
(Lewis and Murray, 1987), 31 of 55 schizophren-
ics showed a total of 50 complications (table 1).
In 13 of 20 healthy controls, a total of 20 complica-
tions occurred. Thus, the schizophrenic group did
not differ from the control group ($\chi^2 = 0.45$, $df = 1$, ns) on the whole. On the “severity weight allocation scale” specific complications
Parnas et al., 1982) 38 chronic schizophrenics had a total of 83 complications during pregnancy
or birth (table II). Eighteen complications occurred in
12 out of 20 normal controls. Compared to the
controls, the total schizophrenic group had the
same frequency ($t = 1.404$, ns), severity ($t = 0.730$, ns), and total score of obstetric complications. The OC levels were not
correlated to gender.

<table>
<thead>
<tr>
<th>Obl imphatic/sporadic distinction according to DSM III-R</th>
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<tr>
<td>The occurrence of complications during pregnancy</td>
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| and birth was the same in familial and sporadic forms of schizophrenia ($z^2 = 2.40$, $df = 1$, ns, table I) as were frequency ($z = 1.058$, ns), severity ($z = 1.427$, ns), and total score ($z = 1.350$, ns) of obstet-
obstetric complications (table II). In addition, both groups were not different from the controls.

Leonhard classification distinguishing between systematic and unsystematic schizophrenia

The occurrence of OCs was the same for both subsamples \( (z^2 = 0.72, df = 1, ns) \). As shown in table II, no significant differences were observed in frequency \( (z = 1.522, ns) \), severity \( (z = 0.090, ns) \) and total score \( (z = 0.362, ns) \) using the Fuchs scale. However, systematic schizophrenics showed a non-significant trend towards an increased frequency of complications in comparison to the controls \( (z = 1.799, P < 0.1) \).

"High genetic risk" group and "low genetic risk" group: (genetic risk supposed to be similar in both classification systems)

Lewis and colleagues (fig 1): In the "high genetic risk" group (schizophrenics who fulfilled the diagnostic criteria of unsystematic schizophrenia and familial schizophrenia), the likelihood of experiencing OCs was significantly less than in the healthy probands \( (z = 3.99, df = 1, P < 0.05) \). Only three out of 13 mothers reported OCs and none of them reported an infectious disease. The "low genetic risk" group (diagnosis of systematic schizophrenia and sporadic schizophrenia) did not have a higher incidence of OCs than controls. However, ten out of 17 mothers reported OCs and there were also seven women who reported infections during pregnancy. In five of the seven mothers the infection was followed by further perinatal complications. Fuchs scale (fig 1): The "high genetic risk group" was not different from the controls. In the "low genetic risk" group, there was a non-significant trend towards an increased frequency of complications (infectious diseases were not considered as compared to normal controls \( (z = 1.651, P < 0.1) \) and the "high genetic risk" group \( (z = 1.748, P < 0.1) \).

Discussion

In order to investigate the incidence of obstetric complications (OCs) in schizophrenia and the relationship of OCs to the development of different disease entities, we interviewed mothers of chronic DSM-III-R schizophrenics (APA, 1987) with severe residual states together with normal age-matched controls in a retrospective study. To be included, patients also had to fulfill the diagnostic criteria of Leonhard's systematic or unsystematic schizophrenia (Leonhard, 1974; APA, 1987). We made use of the methodological approach of Lewis and associates (Lewis and Murray, 1987) and Fuchs (Parnas et al, 1982) which proved to be useful in recording various adverse events in the perinatal and postnatal period.

In the schizophrenic sample as a whole, the level of OCs showed high parallelity, especially to Parnas' original data of schizophrenic patients (Parnas et al, 1982). We failed to find substantial differences in the occurrence of OCs between the diagnostic group of schizophrenia, considered as one disease entity, and normal controls (table I and II). These findings are in keeping with the studies of Turner et al (1986) and Done et al (1991). According to others (Pearson et al, 1985; Nigamankaer et al, 1988; Reddy et al, 1990), our results reveal no difference in the presence and severity of perinatal complications between familial and sporadic forms of schizophrenia. The reported increased incidence of OCs in sporadic schizophrenias (Wili-
the one hand, obstetric complications could be independently noxious events which intensify disturbances caused by infections. On the other hand, severe maternal infectious diseases could increase the likelihood of perinatal complications and, thus, be responsible for the heightened level of OCs in the group “low genetic risk” and in Leonhard’s systematic schizophrasias. The coincidence of maternal infections during gestation and perinatal damage seems to increase the risk of developing chronic, non-genetic schizophrenia in the affected children. Maternal infections are supposed to be significant factors for the deviations of prenatal brain maturation (Jakob and Beckmann, 1986; Mednick et al., 1988). Definite cytotoxic changes in paranuclear structural systems were found in post-mortem brain studies of schizophrenic patients as explained by a disruption of neuronal migration during mid-gestational period (Jakob and Beckmann, 1986; Beckmann and Jakob, 1991; Arnold et al., 1991). Serious obstetric complications point to abnormal cerebral oxidative metabolism and to interrelated hypoxic-ischemic episodes (Hill, 1991; Roth et al., 1992). Anoxia-induced brain damage leads additionally to structurally disturbed maturation and selective cell death (Janowsky and Finlay, 1986).

This study gave rise to the following conclusions: i) in schizophrasias with a low genetic risk, perinatal complications may be of some etiological importance, and ii) in schizophrasias with high genetic risk, perinatal complications do not essentially contribute to the etiology of the disease.

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