Obstetrical Complications, Social Class and Type of Schizophrenia

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Abstract

The emerging neurodevelopmental model posits that prenatal and perinatal factors can play an etiological role in schizophrenia. Consistently, the research on obstetrical complications (OCs) reports an association with the development of more severe schizophrenic symptoms. Low socioeconomic status (SES) has also been linked to both limited prenatal healthcare and to worse prognosis of schizophrenic symptoms. A large sample (n=437) of patients from a state hospital population in the U.S. was screened for study variables. A sequential analysis was conducted, first applying cross tabulations using the chi-square test, and then building separate logit models for poor and nonpoor patients. The cross tabulations indicated an association between OCs and negative symptoms for poor schizophrenic patients, but not for nonpoor patients. Multivariate logit models further supported this result. This is the first study to examine the interaction of OCs, schizophrenic symptomatology and SES of origin.

Key Words: Schizophrenia, Negative Symptoms, Socioeconomic Status, Obstetrical Complications

Introduction

A thorough understanding of the origins of schizophrenia remains elusive, even after more than one hundred years of research (1). One promising line of investigation is the neurodevelopmental model, which posits that prenatal environmental factors and other such stressors are potential risk factors for schizophrenia. More specifically, the model suggests that adverse prenatal and perinatal events can affect critical processes in the genesis of brain structure, which, in turn, predispose an individual to the emergence of schizophrenia later in life (2).

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Evidence supporting the neurodevelopmental model has been generated by many studies with a wide variety of designs. Three principal findings have emerged. First, schizophrenic patients have a tendency for diminished neuromotor, neurocognitive, and behavioral function before the full-blown emergence of the disorder (3-6). Second, schizophrenic patients have an abnormally high prevalence and severity of minor physical anomalies which are ordinarily associated with adverse prenatal events (4, 7). Third, several of the brain abnormalities noted in schizophrenia are present during onset (8, 9). The neurodevelopmental model postulates that genetic factors may play an etiological role, as in the case of mutations and polymorphisms, which also interfere with normal brain development (10). This model also posits that environmental stresses alone, or in combination with genetic factors, can contribute to the genesis of schizophrenia (2, 11).

One type of environmental stressor, obstetric complications (OCs), is a regularly reported correlate of schizo-

Clinical Implications

The central finding of the present study uncovers an interconnection between two risk factors and one outcome variable. The risk factors are obstetrical complications (OCs) and lower socioeconomic status (SES) of origin. The outcome variable is adult schizophrenia with persistent negative symptoms. Specifically, we find that OCs are, in fact, associated with the development of deficit schizophrenia but *only* for patients from impoverished backgrounds. Consistent with the general tenets of the neurodevelopmental hypothesis of schizophrenia (43), the resultant model specifies the environmental location (lower SES) most vulnerable to the prenatal and perinatal incubators of negative schizophrenia. This class-specified finding has important substantive implications. The high prevalence of OCs among those born into poverty can be linked to factors including diminished likelihood of poor pregnant women receiving prenatal healthcare and limited nutritional intake (45, 46). These adverse forces may allow OCs to run their full course, thus producing deleterious developmental effects (47). As noted in the Methods section, the social histories are subject to measurement error, notably on the prevalence of OCs. However, unless these recall errors are concentrated in nonpoor families *and* in families with patients of negative symptomatology—and there is no reason to suspect this is the case—the underestimation of OCs cannot threaten the present finding.

phrenia (12, 13). Numerous studies with different types of designs and samples report that deviations from the normal course of pregnancy and delivery are associated with adult schizophrenia in offspring (11, 14, 15). Since OCs can potentially damage the brain during pregnancy or delivery (16), they may be more common in schizophrenia patients with early age of onset. Indeed, a meta-analysis based on the data of eleven research groups indicates that schizophrenic patients with early onset are much more likely than their later-onset counterparts to have had their gestation or birth complicated by an OC (17).

If OCs have the potential to cause brain damage, it is possible that OCs may also connect with type of schizophrenia. Indeed, schizophrenia with negative symptoms—a condition connected with poor prognosis and diminished responsiveness to medications compared to schizophrenia with positive symptoms—has been linked with an abnormality in the actual structure of the brain (18, 19). This is a compelling reason why negative symptomatology is included as a major variable in this study. To date, there has been a paucity of studies examining *type* of schizophrenia and OCs (20). Here we refer to type of schizophrenia in two ways, according to types of symptoms: negative form and positive form.

Are there environmental factors connected to OCs which may increase the likelihood of negative schizophrenia? We hypothesize that one such factor is lower social class of origin. Poverty may not only be related to the likelihood of OCs, but also permits them to run their full course. A meta-analysis of the association between lower socioeconomic status (SES) and schizophrenia reports that lower SES is clearly linked with elevated risk for schizophrenia *in general* (21). More specifically, lower SES at birth is also related to an especially bad outcome as evidenced by clinical assessments of chances for recovery among schizophrenic patients from impoverished backgrounds (22, 23). Our recent research demonstrates a significant connection between lower SES at birth and *type* of schizophrenia, specifically the negative form (24). Being born into an economically deprived household increases the likelihood of exposure to a host of risk factors, including poor prenatal healthcare (24). Inadequate healthcare during gestation could be of special significance to the risk of OCs, which, in turn, could impact early brain development (12, 16).

The research findings cited above constitute a logical fit with the neurodevelopmental model of schizophrenia. That is, the data suggest an interconnection between obstetrical complications, lower SES of origin and negative schizophrenia. Thus, the major hypothesis of the present study is that negative schizophrenia is elevated among patients born to impoverished mothers who suffered obstetrical complications. It is important to note that this study is rare and novel. It is rare because there are few studies examining the role of OCs in relation to symptoms of schizophrenia (20); it is novel because it is the first study to simultaneously examine the interaction of OCs and symptoms with SES of origin.

Methods

Data for this study have been taken from the cumulative anonymous medical records of 437 schizophrenic patients discharged from Norristown State Hospital (NSH) in Pennsylvania (United States) between 1984 and 1990. Diagnostic procedures employed multidisciplinary evaluations with periodic review. Specific criteria for index diagnosis are based on the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM)* (25).

Upon admission, patients were evaluated by staff psychiatrists and other members of a multidisciplinary team within forty-eight hours for diagnosis and treatment plan purposes. Later, diagnostic reviews were conducted for each patient every three months, or as needed, during hospitalization. Since some patients have been discharged and

readmitted over time, we employed a combination of three operational measures to enhance longitudinal analysis of symptom stability. The measures included clinical assessments by NSH staff at intake and during last hospital stay, as well as *DSM* diagnosis at last discharge.

Clinical Assessments

In addition to diagnosis by *DSM* standards, NSH staff professionals further categorize patients into negative (e.g., symptoms such as mutism) and positive (e.g., symptoms such as hallucinations) subtypes. Subtyping is based on diagnosticians' judgments of clear presentation of positive or negative features at intake and during last hospital stay. Classification into these subtypes is based on positive and/or negative features of many individuals with schizophrenia (26). It is also compatible with research centering on "deficit/nondeficit schizophrenia." Deficit schizophrenia is an older terminology used to describe long-term patients with a persistent negative presentation. The division of schizophrenia into either "deficit/nondeficit" or "negative/positive" subtypes has yielded many important substantive findings about schizophrenia (27-29). Subtyping in this study is enhanced by chart materials with detailed patient symptomatology.

In addition to subtyping drawn from patient files, a number of positive and negative scales have been retrospectively applied from chart materials. They include the Scale for the Assessment of Negative Symptoms (SANS) (30), the Scale for the Assessment of Positive Symptoms (SAPS) (30), and the Positive and Negative Syndrome Scale (PANSS) (31). Although some may question the validity and reliability of chart-based assessments of negative and positive symptoms, we do not think these are serious problems in this study. It was standard procedure at NSH to require that interviewer observation of the patient be completely and directly recorded onto the charts. Therefore, the clinical assessments were solely conducted by NSH staff professionals, and we retrospectively applied the identical assessments to our sample. Both the original assessments at NSH and our replication of those assessments were conducted independently of patient history of OCs. The literature reports that the retrospective application of the SANS, SAPS and PANSS can be completed from chart materials if the latter are sufficiently detailed (32, 33). Such was the case in the present study.

One of the issues we faced was how to deal with diagnoses that changed over time. This proved to be a minor problem, since this type of discrepancy rarely occurred and, when it did occur, we simply eliminated the case from the sample. Thus, diagnosis is operationalized from three temporal sources: clinical assessment at first intake, during last hospital stay, and *DSM* diagnosis at last discharge. The temporal points of these measurements not only permit the observation of symptom stability over time, but also reflect studies cited earlier that schizophrenia patients who show *persistent* negative symptoms are an important subgroup with low-remission rates (18, 34-37).

Negative/positive assessments were conducted by three independent raters. Two of the raters are experts in the field; one is a clinical psychologist and the other is a psychiatric sociologist. Consensus was reached on the classification of all included cases. Thus, interrater reliability is one hundred percent because, in the rare instances where there was disagreement, the cases were dropped. No evidence of extrapyramidal complications is present.

As noted above, patients who did not clearly present as negative or positive were not included in this study. Thus, a patient was cross verified as negative only if chart materials reflected presentation of negative symptoms at first admission and during the last hospital stay and the index diagnosis was *DSM* "chronic" at discharge.

SES Classification

Epidemiological analyses of SES and risk of schizophrenia are often confounded by the "social stress" versus "social drift" controversy. This study is not compromised by the debate, since SES is only assessed at the time of patients' births. This provides a direct measure of a potential risk factor connected to SES of family of origin (21).

Information about the SES of the patients is contained in the "social history" section of their hospital records. The social history often includes detailed accounts of the family into which the patient was born. The histories were compiled at intake by psychiatric social workers from personal interviews with first-degree relatives. These verbal accounts often provide specific information about SES, such as the occupation, income status and level of education of family head(s).

Researchers using occupational scales to rate SES frequently dichotomize social class into higher and lower class groups (38, 39). Because this study hypothesizes that membership in the lower social class may result in a more severe (negative) form of schizophrenia, the sample is bifurcated into poor versus nonpoor categories at the time of the patient's birth. SES classification was facilitated by the application of the Occupational Distributions of the U.S. Bureau of the Census (40). This classification scheme is comprehensive and also temporally matches the time span of our data set. Whenever nonoccupational information was available in the social histories (e.g., "the family was well-off financially"), it is used to facilitate the dichotomous classification. Low SES ("poor") includes the indigent, the unemployed and unskilled laborers; high SES ("nonpoor") generally con-

sists of skilled laborers and above. Thus, the final sample is comprised of 437 cases which have been carefully delineated by both schizophrenic subtype and SES categorized as poor versus nonpoor.

Obstetrical Complications

Like SES, data about OCs were obtained from the "social history" section of the hospital records. Nine obstetrical complications appeared in these accounts: maternal health problems during pregnancy, prenatal alcohol abuse, prenatal drug abuse, prenatal violence, premature birth, unusually long labor, breech birth, forceps delivery, and other delivery complications. Each OC was rare, almost always in single digit percentages; this rendered statistical tests of any particular complication untenable.

Prevalence of obstetrical complications was probably underestimated in the social histories due to recall problems since, by the time of admission, several decades would have elapsed since the patients were born. Obstetrical histories were provided by first-degree relatives, which usually, but not always, included the patient's mother. There was an interview format which included questions about OCs. Studies of the effect of maternal recall bias of OCs in research on schizophrenia have produced mixed results. One study suggested that schizophrenic patients had higher rates of OCs recalled by their mothers than controls (41). Another study found no evidence of positive recall bias as mothers of offspring with schizophrenia reported fewer complications than indicated on their obstetric records (42). Additionally, there is no reason to believe that recall bias in the present study will differentially affect the other variables (SES and symptomatology) in the research model to produce misleading effects.

Data Analysis

The dependent variable is dichotomous, coded as 0=positive and 1=negative schizophrenia. Included in the research model are the dichotomous measure of social class described above (poor vs. nonpoor), and two different breakdowns of OCs. The simplest of the latter is an assigned dichotomy, separating schizophrenic patients with any obstetrical complications—i.e., receiving a "1" code for any of the nine identified above—from those with no complications recorded. This is the version that will be utilized in the first stage of the analysis in cross tabular comparisons of effects for poor versus nonpoor patients.

The second stage of the analysis employs multivariate logit models incorporating a more precise measure of the obstetrical complications variable (43). A simple additive index yielded sums ranging from 0 to 4 OCs for the schizophrenic sample. Also entered into the models are race (white vs. nonwhite) because of its possible association with risk of schizophrenia in the limited literature (23), and sex, because related analyses by this research team (44) suggest differential rates of deficit versus nondeficit risk for males versus females.

Results

Cross Tabular Analysis

Table 1 exhibits the cross tabulation of obstetrical complications by schizophrenic subtype for the full sample (n=437). Note that 27.1% of schizophrenics with no obstetric complications ("Absent") are classified as "Negative" type, compared to 34.8% with the "Negative" classification for schizophrenic patients with obstetrical complications "Present." This excess of negative diagnoses among patients with OCs is suggestive, but does not attain statistical significance in the chi-square test (X^2=2.423, p=.120).

Table 1 Type of Schizophrenia by Obstetrical Complications

	Type of Schizophrenia (n=437)	
Obstetrical Complications	**Positive**	**Negative**
Absent	237 (72.9%)	88 (27.1%)
Present	73 (65.2%)	39 (34.8%)

X^2=2.423, p=.120

The derived hypothesis, of course, specifies the tested association by social class. Table 2 duplicates the cross tabulation for poor schizophrenic patients, and the results are more than suggestive. The observed excess of negative diagnoses among poor patients with obstetrical complications "Present" versus "Absent" (42.9% vs. 29.0%) yields a statistically significant chi-square value (X^2=4.409, p=.036). The identical comparison for nonpoor schizophrenic patients in Table 3 does *not* attain significance (X^2=0.164, p=.686), as the close match of negative diagnoses would imply (24.5% vs. 21.4%).

Logit Models

The cross tabular findings provisionally support a social class-specified effect of obstetrical complications upon schizophrenic subtype. They are only provisional, however, because the relatively robust chi-square test (clearly advantageous here because of weak parametric assumptions) is at a disadvantage in partitioning multivariate effects. For that

Table 2 Type of Schizophrenia by Obstetrical Complications for Poor Patients

	Type of Schizophrenia (n=256)	
Obstetrical Complications	Positive	Negative
Absent	132 (71.0%)	54 (29.0%)
Present	40 (57.1%)	30 (42.9%)
X^2=4.409, p=.036		

Table 3 Type of Schizophrenia by Obstetrical Complications for Nonpoor Patients

	Type of Schizophrenia (n=181)	
Obstetrical Complications	Positive	Negative
Absent	105 (75.5%)	34 (24.5%)
Present	33 (78.6%)	9 (21.4%)
X^2=0.164, p=.686		

reason, the analysis now proceeds to the construction of logit models. The cross tabular results, in effect, constitute a *prima facie* case for building a separate model for poor and nonpoor patients; these models will each be further specified by sex and race.

Table 4 Logit Model for Poor Patients

Variable	Beta Coefficient	Standard Error	Odds Ratio	Probability
Sex	-0.167	0.311	0.847	0.296
Race	-0.050	0.290	0.951	0.431
Obstetrical Complications	0.342	0.175	1.383	0.032
(Constant)	-0.560	0.624	—	0.185

Table 4 presents the results of the logit model for poor schizophrenic patients. Note immediately the positive odds ratio (1.383) and the statistically significant logistic regression coefficient (p=.032) for the obstetrical complications variable. These results are consistent with higher risk of negative schizophrenia accompanying higher occurrence of OCs among poor patients. Note also that sex and race do not register statistical significance.

Table 5 Logit Model for Nonpoor Patients

Variable	Beta Coefficient	Standard Error	Odds Ratio	Probability
Sex	0.783	0.384	2.189	0.021
Race	0.016	0.552	1.016	0.489
Obstetrical Complications	-0.010	0.281	0.990	0.486
(Constant)	-2.175	0.895	—	0.008

In Table 5 for nonpoor schizophrenic patients, obstetric complications show the anticipated noneffect (p=.486). Although it is included in the models here as a control variable, it should be duly noted that sex is statistically significantly related to the negative/positive diagnosis among nonpoor patients (p=.021). This effect is explored by the authors in a separate report (44).

Therefore, the multivariate logit models provide confirmatory evidence for the case established by the cross tabulations. The central finding is that *obstetrical complications do carry a heightened risk of negative diagnosis among schizophrenics born into poverty.*

Discussion

The central finding of the present study uncovers an interconnection between two risk factors and one outcome variable. The risk factors are OCs and lower SES of origin. The outcome variable is adult schizophrenia with persistent negative symptoms. Specifically, we find that OCs are, in fact, associated with the development of deficit schizophrenia but *only* for patients from impoverished backgrounds. Consistent with the general tenets of the neurodevelopmental hypothesis of schizophrenia (2), the resultant model specifies the environmental location (lower SES) most vulnerable to the prenatal and perinatal incubators of negative schizophrenia.

This class-specified finding has important substantive implications. The high prevalence of OCs among those born into poverty can be linked to factors including diminished likelihood of poor pregnant women receiving prenatal healthcare and limited nutritional intake (45, 46). These adverse forces may allow OCs to run their full course, thus producing deleterious developmental effects (47). As noted in the Methods section above, the social histories are subject to measurement error, notably on the prevalence of OCs. However, unless these recall errors are concentrated in nonpoor families *and* in families with patients of negative symptomatology—and there is no reason to suspect this is the case—the underestimation of OCs cannot threaten the present finding.

Expanded knowledge of the role of prenatal stressors has important implications for understanding the complex etiology of schizophrenia. Here we provide sufficient evidence to warrant further studies of the interconnections between OCs, SES, and type of schizophrenia. Research employing different data sets is necessary to firmly establish our finding as a definitive marker of the pathogenesis of schizophrenia. Additionally, more sharpened analyses, including possible variation by sex, may be especially revealing. Many analyses of risk factors fail to specify diagnosis, instead classifying schizophrenia as a general condition; others clump the entire spectrum of schizophrenia disorders into one category. This study measures schizophrenia by subtype, and screens for changing symptomatology over time. To our knowledge, this is the first study of its kind to longitudinally evaluate schizophrenic subtype while also assessing SES of birth family and obstetrical complications.

The data set employed in this study has shortcomings. Detailed information was available to separate patients into negative/positive categories and to eliminate cases with mixed symptomatology. However, sample size was limited by excluding cases with insufficient specifications for valid SES classification. Additionally, our data set only includes patients from a single state mental hospital in the northeastern United States. Consequently, the national and cross-cultural generalizability of the sample (n=437) is not known. On the other hand, a major strength of this study is that multivariate data sources of this kind are rarely available at all in the professional literature in samples of this magnitude.

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