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Clinical Polydiagnostic Studies in a Large Swedish Pedigree with Schizophrenia

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Summary. A polydiagnostic computerized diagnostic system for psychosis was used in a Swedish family complex, and 51 patients with psychiatric symptomatology were examined with eight main diagnostic systems for schizophrenia and three systems for schizophrenic subgroups. All patients fulfilled the criteria for schizophrenia according to Taylor et al., 50 according to Carpenter, 41 according to RDC, and 31 of the 51 according to DSM-III and DSM-III-R. The hypothesis that the patients in the Swedish family complex differ from other phenotypes of schizophrenia must be refuted based on the data of the present study.

Key words: Families – Genetics – Polydiagnostic approach – Schizophrenia – Swedish family complex

Introduction

Schizophrenia is a mental illness that affects about 1% of the human population at some stage in their life. The "schizophrenias" have historically included larger diagnostic groups than today, since diseases with schizophrenia-like symptoms, such as general paresis, brain trauma, neoplasia. Huntington's disease, acute porphyria and chromosomal aberration are now usually classified separately from "true" schizophrenia, which is considered to occur in the absence of "coarse brain disease" (Schneider 1959). Recent genetic linkage studies suggest that the genetic factors underlying schizophrenia may be heterogeneous. Different genotypes may or may not correspond to differences in phenotype (Gurling 1989). With the new possibility of classifying schizophrenic illness at the molecular genetic (i.e. DNA) level, there is an urgent need for generally available and accepted methods for systematic subclassification of phenotypes in families with schizophrenia and related schizophrenia-like diseases. Several diagnostic systems to describe the clinical features of schizophrenia have been used, but no single system has so far gained general acceptance. Until more information is gathered, one approach is to use several diagnostic systems simultaneously. This approach has been applied in the present study of a Swedish family complex presently being investigated for DNA linkage (Kennedy et al. 1988, 1989).

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Materials and Methods

Materials

The families under study comprise a previously documented Swedish kindred with many cases of schizophrenia first described by Böök (1953) and more recently by Wetterberg and Modrzewska (1989). Epidemiological and genealogical data about the families have been gathered from local hospital and parish records and through extensive personal interviews with patients and healthy family members by one of us (LW) over more than a decade. Diagnostic information has been obtained from medical records and examination of the patients and their relatives in their homes. The majority of the patients were also examined by several other psychiatrists for extended periods during hospitalization and out-patient aftercare. In addition, the clinical evaluation drew on case note review for life-time diagnosis, including all the information mentioned above.

In the present study of 51 patients with psychiatric symptoms from the large Swedish family under investigation, sufficient clinical data were obtained and DNA secured. The material comprised 31 men (27–72 years of age) and 20 women (30–80 years of age). The age at onset for the men ranged from 13 to 37 years, and 10 had age at onset before 20 years. Among the women the range of age at onset was 9–38 years, 11 having experienced onset before the age of 20 years.

Methods

The different classification systems for schizophrenia used in the present study have been evaluated using a computerized program named OPCRIT, developed by McGuffin et al. (1990). OPCRIT is based on an extended version of an operational criteria checklist for psychotic illness (OCCPI) to facilitate a "polydiagnostic" approach to the classification of schizophrenia (McGuffin et al. 1984). Each patient was rated for the presence or absence of 74 items using a checklist of the specific criteria. The checklist was extracted from nine sets of commonly used operational criteria for schizophrenia (Schneider 1959; Feighner et al. 1972; Carpenter et

al. 1973; Tsuang and Winokur 1974; Spitzer et al. 1975; Taylor et al. 1975; DSM-III 1980; Pichot 1984; DSM-III-R 1987). Where items were present in more than one set of criteria with closely similar specifications, these were condensed into a single item. The specification for each item had previously been agreed upon by the different investigators on the basis of their originally published criteria for the various diagnostic systems. The checklist was scored from all available data of the family members, with "1" for the presence and "O" for the absence of each item. The reliability of the criteria had previously been studied using 20 case reports that had been rated by two psychiatrists. They obtained good agreement with a mean kappa over all items of 0.77 (Farmer et al. 1983). Subsequent studies based upon more extensive material and using multiple raters have confirmed that reliability is highly significant.

Results

Using the OPCRIT program of McGuffin et al. (1990), 51 patients with psychiatric symptoms were examined. All 51 patients fulfilled the criteria for schizophrenia according to Taylor et al. (1975), 50 according to Feighner et al. (1972), 50 according to Carpenter et al. (1973), 41 the narrow schizophrenia of Schneider (1959) and 41 RDC and 31 patients DSM-III and DSM-III-R criteria for schizophrenia (Table 1). Of the 51 patients who did not fullfil the criteria for schizophrenia 1 was classified as probable schizophrenia according to Feighner et al. (1972), 1 as broad schizophrenia and 9 as schizoaffective according to RDC, and 16 atypical and 4 as schizoaffective according to DSM-III (Table 2). The 51 patients were also classified according to subgroups: 50 were rated as undifferentiated according to Tsuang and Winokur (1974), 41 as having mixed and 9 type I schizophrenia according to Crow (1980); and 23 in group P and 28 in group H according to the subgrouping of Farmer et al. (1983).

Table 1. Diagnoses for 51 patients with psychiatric symptoms belonging to a Swedish pedigree

n Diagnosis	Diagnostic system
51 Schizophrenia	Taylor et al. (1975)
51 Delusional attack	Pichot (1984)
50 Definite schizophrenia	Feighner et al. (1972)
50 Schizophrenia	Carpenter et al. (1973)
49 Narrow schizophrenia	Schneider (1959)
41 Narrow schizophrenia	Spitzer et al. (RDC) 1975
31 Schizophrenia	DSM-III (1980)
31 Schizophrenia	DSM-III-R (1987)

Table 2. Diagnoses for those of the 51 patients belonging to a Swedish pedigree who did not fullfil the criteria for schizophrenia. (For reference to diagnostic systems see Table 1)

n Diagnosis	Diagnostic system
1 Probable schizophrenia	Feighner et al. (1972)
1 Broad schizophrenia	RDC
9 Schizoaffective	RDC
16 Atypical psychosis	DSM-III
4 Schizoaffective	DSM-III-R

Discussion

Reliable and valid diagnoses are essential if genetic linkage studies are to be successful. The development of more specific therapies and the possibility of diagnostic subgrouping at the molecular level also mean that diagnostic definitions have become even more important. This includes description of the phenotypes in schizophrenic families, and different studies are dealing with this problem using different strategies. In the present study we have included several diagnostic systems into a polydiagnostic approach. The Swedish family complex described here includes several patients with psychotic-type symptoms. The phenotype seems to be inherited in an autosomal dominant fashion, and linkage studies may be performed in these families only on this basis. The question as to whether the large Swedish pedigree includes a specific genetic type of psychoses not related to other types of schizophrenia can possibly be answered in the future using combined clinical and molecular techniques. At present, according to the polydiagnostic method, the hypothesis that the phenotype of schizophrenia in the Swedish families may differ from other phenotypes of schizophrenia in terms of clinical features must be refuted, since there is a significant agreement of the clinical schizophrenic phenotype of the Swedish patients when the phenomenology is compared in several diagnostic systems.

Although a pure monozygotic hypothesis, where a single locus accounts for all concordence between relatives has been discussed (McGuffin et al. 1987; McGue and Gottesman 1990), a major locus with a multifactorial background remains a distinct possibility. Our continued studies are proceeding on the assumption that there is a

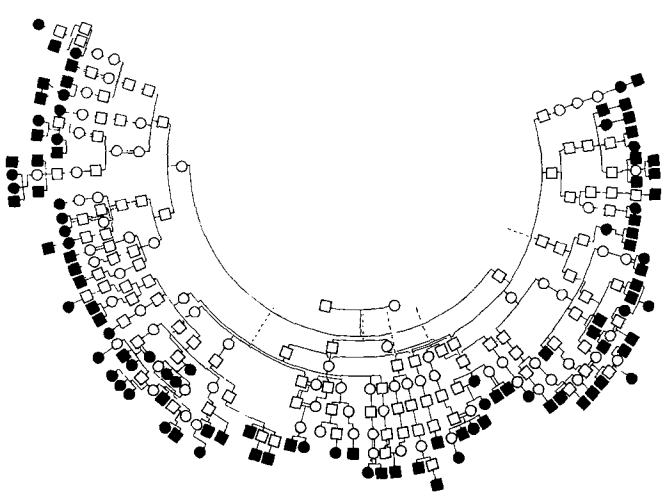

Fig. 1. Pedigree of the families from Sweden demonstrating the relationship between the majority of the examined patients used in the present polydiagnostic study. The non-schizophrenic siblings are not shown. *Filled symbols* represent schizophrenic patients, *black squares* for men and *black circles* for women. *Double lines* represent consanguineous marriage

major gene operating with a strong enough effect on the phenotype of schizophrenia to make it detectable by linkage strategies. This does not exclude the possibility that several different mutations may cause the schizophrenic phenotype, in a similar way as has been shown for the phenotype of acute intermittent porphyria (Wetterberg 1978; Grandchamp et al. 1989; Lannfelt et al. 1989).

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