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Age-specific familial risks of psychotic disorders and schizophrenia: A nation-wide epidemiological study from Sweden

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Abstract

Objective: This study analyzed men and women separately by age at hospital diagnosis of psychotic disorder or schizophrenia and by maternal or paternal disease after taking several possible confounders into account.
Methods: The Multigeneration Register, in which all men and women born in Sweden from 1932 onwards are registered together with their parents, was linked to hospital data. This yielded 21,199 male and 19,029 female cases of psychotic disorders in addition to 12,799 paternal and 23,021 maternal cases of psychotic disorders (including schizophrenia). Standardized incidence ratios (SIRs) were calculated as the ratio of observed and expected number of cases among men and women with mothers and/or fathers affected by psychotic disorders or schizophrenia, compared with men and women whose mothers and/or fathers were not affected by psychotic disorders or schizophrenia.
Results: The overall significant SIRs among men and women with a mother, father or both parents hospitalized for psychotic disorder varied between 2.86 and 20.30. Maternal transmission of psychotic disorder was stronger than paternal, and the highest SIRs were found in the youngest age groups. Similar results were found when the subgroup schizophrenia was analyzed separately. Maternal or paternal schizophrenia implied higher risks for the offspring than maternal or paternal psychotic disorders.
Conclusions: Hereditary factors have a strong influence on the onset of psychotic disorders and schizophrenia. Young people and individuals with both parents affected by these diseases need special attention as their SIRs were particularly increased.

Keywords: Familial risk; Genetics; Hereditary factors; Psychotic disorders

1. Introduction

Psychotic disorders are severe and relatively common neuropsychiatric disorders characterized by mental dysfunction across multiple domains of the brain. This occurs in about 1% of the world's general population. Although the exact etiology of the disorder is not understood, family, twin and adoption studies have suggested that genetic factors play a major role in the transmission of psychotic disorders. In a Danish cohort study, a 3.22-fold risk of psychotic disorders was observed among first-degree relatives (Laursen et al., 2005). From twin studies, the heritability of psychotic disorders was estimated to be over 80% (Cannon et al., 1998; Cardno et al., 1999). Previous

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studies also indicate that first-degree relatives of people with schizophrenia have a higher risk of psychotic disorders than first-degree relatives of control persons without psychotic disorders (2–9% and 0–1%, respectively) (Shih et al., 2004). Results from family and epidemiological studies have led to the suggestion that early-onset psychotic disorders may be more strongly genetically influenced (Alda et al., 1996; Kendler and MacLean, 1990; Pulver et al., 1990; Waddington and Youssef, 1996). These findings have not been reported consistently (Maier et al., 1993; Sham et al., 1994). The influence of genetic factors has been reported to have a significantly higher effect in women than men in some studies (Maier et al., 1993) but not in others (Albus and Maier, 1995; Cannon et al., 1998; Laursen et al., 2005). Consequently, there is a need for further research into the genetic etiology of psychotic disorders and schizophrenia with specific attention paid to age and sex effects.

The patterns of inheritance of psychotic disorders are probably complex. Environmental factors are also important in the development of psychotic disorders, which is based on recent research of the association between psychotic disorders and cannabis use, childhood trauma and urbanicity (Cougnard et al., 2007). A study of Finnish adoptees found evidence for a genotype–environment interaction in schizophrenia-spectrum disorders (Tienari et al., 2004).

For the future success of gene identification efforts, it is important that the familial risks are characterized in detail. It has been suggested that "age of onset is the single most important characteristic of schizophrenia that could yield clues to its origin" (DeLisi, 1992). We examined age-specific familial risks for psychotic disorders and schizophrenia using the nationwide Swedish MigMed Research Database. The novel contribution of this study is partly its approach; it was based on a nationwide register of all hospitalized cases in Sweden between 1987 and 2004, which yielded a substantial number of cases in two generations. Second, the use of hospitalized cases eliminated potential self-report and recall bias. Swedish data on medically diagnosed psychotic disorders were obtained from register sources with virtually complete coverage. In addition, the Swedish Multigeneration Register is a well-validated source that has been found to be reliable in the study of many familial diseases (Hemminki et al., 2005; Hemminki et al., 2006; Sundquist et al., 2004). This study examined age-specific familial risks among men and women with a mother and/or father with psychotic disorder or schizophrenia after adjustment for several confounders.

2. Materials and methods

2.1. MigMed research database

Data used in this study were retrieved from the MigMed database, located at the Center for Family and Community Medicine at the Karolinska Institute in Stockholm. MigMed is a single, comprehensive database that has been constructed using several national Swedish data registers, including but not limited to the Total Population Register, the Multigeneration Register, and the Swedish Hospital Discharge Register (1987–2004) (Rosen and Hakulinen, 2005; Statistics Sweden, 2005; The National Board of Health and Welfare). Information from the various registers in the database is linked at the individual level via the 10-digit national registration number assigned to each person in Sweden for his or her lifetime. Prior to inclusion in the MigMed database, national registration numbers were replaced by serial numbers to ensure the anonymity of all individuals.

Since the database contains information from the Multigeneration Register, it is possible to link more than 9 million index persons (persons born in or after 1932 and registered in Sweden at any time since 1961) with their biological parents, i.e. more than 3.2 million families. The latest version of the Multigeneration Register, which has been incorporated in the MigMed database, includes supplementary data from church records on index persons domiciled in Sweden between 1947 and 1961.

2.2. Outcome variable

Hospitalization for psychotic disorders was retrieved from hospital discharge records reported according to the 9th (1987–1996) and 10th (1997–2004) versions of the International Classification of Diseases. The following ICD codes were included for psychotic disorders, i.e. schizophrenia, schizotypal and delusional disorders: ICD-9: 295 (schizophrenic disorders), 297 (paranoid states), and 298 (other nonorganic psychoses); ICD-10: F20 (schizophrenia), F21 (schizotypal disorder), F22 (persistent delusional disorders), F23 (acute and transient psychotic disorders), F24 (induced delusional disorder), F25 (schizoaffective disorders), F28 (other nonorganic psychotic disorders), and F29 (unspecified nonorganic psychosis). The subgroup schizophrenia was analyzed separately (ICD-9: 295 and ICD-10: F20 and F21).

2.3. Individual variables

Gender: men and women.

Age at diagnosis was categorized in 5-year groups and the groups were merged as necessary.