Association between family history of psychiatric disorders and long-term outcome in schizophrenia – The Northern Finland Birth Cohort 1966 study

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A B S T R A C T

Family history of psychiatric disorders has been associated with impaired outcome in schizophrenia, but very few studies have investigated its long-term social and occupational outcome. We investigated the association of family history of psychiatric disorders, especially psychosis, with long-term social, occupational, clinical and global outcome in schizophrenia. The study sample comprises of the Northern Finland Birth Cohort 1966. Cohort members with psychosis were detected by Finnish national registers. Altogether 69 individuals with schizophrenia spectrum diagnosis participated, mean age 43, after on average 17 years since onset of illness. The information regarding family history of psychiatric disorders were gathered from registers and interviews. A Strauss-Carpenter Outcome Scale, PANSS and SOFAS were conducted to assess the outcome. Results showed that the family history of any psychiatric disorder was associated with more severe positive and emotional symptoms in PANSS. The family history of psychosis was not associated with outcomes. These findings suggest that family history of psychiatric disorders has a small association with outcome in schizophrenia. Despite family history of psychosis being a strong risk factor for schizophrenia, after years of illness it does not seem to affect outcome.

1. Introduction

Genetic factors have a major role in the aetiology of schizophrenia, as suggested by adoption, twin and family studies (Tsuang et al., 1991). Family history of schizophrenia is considered to be the strongest risk factor for schizophrenia with a 6.6–9.9 relative risk among first-degree relatives (Mortensen et al., 2010; Lichtenstein et al., 2009). So far the studies have not been able to identify a single gene that would have a large effect on the risk of schizophrenia, and a recent genome-wide association study reported 108 schizophrenia-associated genetic loci (Ripke et al., 2014). The emerging epigenetic research provides a further interesting aspect to the matter (Shorter et al., 2015; Ibi et al., 2015).

Outcome in schizophrenia is heterogenous (Morgan et al., 2014; Lang et al., 2013), and full recovery is relatively rare, 13.5% (Jääskeläinen et al., 2013). Many patients have deficits in social and occupational functioning (Marwaha and Johnson, 2004; Warner, 2004). Unfortunately, during the last decades, the proportion of social recovery (Warner, 2004) and full recovery (Jääskeläinen et al., 2013) in schizophrenia has not increased.

The results on the association between family history of any psychiatric disorder and outcome in schizophrenia are varying.
Family history of psychiatric disorders has been associated with more psychopathological symptoms at a two-year follow-up and more rehospitalizations in a five-year follow-up (Feldmann et al., 2001), higher risk of relapse, but, interestingly, slightly less severe scores of psychopathology and a better attitude towards pharmacotherapy in a one-year follow-up (Ciudad et al., 2012). On the other hand, the number of relapses in a seven-year follow-up period did not differ based on psychiatric diagnoses in relatives (Altamura et al., 2001).

The earlier literature has often considered the family history of psychosis a sign of poor outcome in schizophrenia, although there are not many studies to support this reckoning (Bromet et al., 2005; Esterberg et al., 2010; Käkelä et al., 2014). Esterberg et al. (Esterberg et al., 2010) studied specific dimensions of clinical outcome in a meta-analysis, stating that family history of psychosis has a small but statistically significant impact on more severe negative symptoms, and small and non-significant impact on positive symptoms. We have previously investigated the association between family history of psychosis and occupational, social and global (i.e. combined occupational, social and clinical) outcome in schizophrenia in a meta-analysis (Käkelä et al., 2014). According to our review, family history of psychosis has a relatively small but statistically significant association with poor long-term occupational and global outcome. However, there were quite few studies focusing on these outcomes. In particular, there were no studies that focused on social outcome. Thus, research on the specific outcomes in schizophrenia is needed.

It is highly important to find predictors of poor social and occupational outcomes to have a better understanding of the factors that affect the prognosis of schizophrenia. Since patients with psychiatric family history are a possible target group for intervention, it is sensible to investigate the importance of the association between family history of psychiatric disorders and outcome in schizophrenia. In the current study the outcome is investigated thoroughly including several dimensions of outcomes, i.e. social, occupational, clinical and global aspects, with long-term follow-up in a general population sample. In addition, to our knowledge this is the first study that investigates the association between family history of psychosis and social outcome in schizophrenia.

We aimed to study how family history of psychiatric disorders, and especially psychosis, affect long-term social, occupational, clinical and global outcome in schizophrenia in a longitudinal population-based cohort. Our hypothesis was that family history of psychiatric disorders, especially psychosis, is associated with poorer long-term outcome.

### 2. Methods

#### 2.1. Study population

The subjects of the study were members of the Northern Finland Birth Cohort 1966 (NFBC 1966). The NFBC 1966 is a general population based sample of 12,068 pregnant women and their 12,058 children with an expected delivery date during 1966 in two northern provinces of Finland: Lapland and Oulu (Jaaskelainen et al., 2015). Altogether 10,934 of these subjects, who were living in Finland at the age of 16, gave consent for their data to be used. The Ministry of Social and Health affairs gave permission to gather the data, and the Ethical Committee of the Northern Ostrobotnian Hospital District approved the study design.

The NFBC 1996 cohort members with psychosis were identified by using the nationwide Care Register for Health Care (CRHC) and the registers of the Finnish Social Insurance Institute. The CRHC was utilized to identify the individuals who had developed psychosis until 2008. The CRHC covers all mental and general hospitals and in-patient wards at local health centres and private hospitals. To find patients who were also treated only as outpatients, the registers of the Finnish Social Insurance Institute were used to find subjects diagnosed with psychosis by the end of year 2008, i.e. subjects with sick leave or disability pension due to psychosis or entitled to reimbursable medication due to a psychotic disorder. The diagnoses of psychosis made before 1998 were validated by using hospital notes (Isohanni et al., 1997; Moilanen et al., 2003), and the diagnoses made between 1998 and 2008 relied on the register data. Based on all this information, 266 cohort members with the diagnosis of psychosis and known address were asked to participate in a psychiatric study performed in 2008–2011, approximately at the age of 43 years (Nykänen et al., 2016).

The psychiatric study included an interview that took place in 2008–2011 at the Oulu University Hospital, Oulu, Finland. The Structured Clinical Interview for DSM-IV (SCID I – interview; First et al., 2002) resulting in DSM-IV diagnoses was conducted for all participants. Based on the SCID I – interview and registers, 69 participants had schizophrenia spectrum disorder (57 schizoprenia, 2 schizophreniform, 8 schizoaffective and 2 delusional disorder). The participation flow is presented in Fig. 1.

#### 2.2. Outcome data

To assess the different aspects of outcome (i.e. social, occupational, clinical and global), we used the Strauss-Carpenter Outcome Scale, PANSS (Positive and Negative Syndrome Scale; Kay et al., 2000) and SOFAS (Social and Occupational Functioning Assessment Scale; Spitzer et al., 2000) outcome measures, which are widely used and provide a comprehensive overview of the outcome. As a part of the interview at the age of 43 the Strauss-Carpenter Outcome Scale – interview (Strauss and Carpenter, 1977) was conducted, which has been established as an outcome assessment tool (Nieman et al., 2012). It includes the following questions:

![Fig. 1. Flowchart of participation of the individuals.](image-url)
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