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Can positive family factors be protective against the development of psychosis?

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ABSTRACT

Genetic and environmental factors are both involved in the aetiology of psychotic disorders. The aim of this study was to assess if positive and negative environmental factors, together with psychotic family antecedents, are associated with the recent development of psychosis. We also investigated the interactions between family history of psychosis and positive and negative family environment. The sample comprised 110 children and adolescents, who had suffered a first psychotic episode and 98 healthy controls. All subjects were interviewed about their socioeconomic status, family history of psychosis and family environment (Family Environment Scale, FES). Early onset psychosis was significantly associated with a family history of psychosis. Family environment was perceived as more negative and less positive among patients than among controls. A negative family environment increased the risk of psychosis independently of the family history of psychosis. However, there was a significant protective effect of a positive family environment for persons with a family history of psychosis. This effect was not seen in subjects without a family history of psychosis. Therefore, our results support the importance of considering both family history of psychosis and family environment in the early stages of psychosis.

1. Introduction

The aetiology of psychotic disorders has been related to a neurodevelopmental disorder. This abnormal development of the central nervous system is thought to be associated with both genetic and environmental factors present in the early stages of foetal development, and with environmental factors that are present during early life. The presence of a genetic risk for psychosis does not mean development of the disease is inevitable, as only some of the vulnerable population will develop a psychotic disorder. Until recently, genetic studies gave little information about the aetiology of psychosis (European Network of National Schizophrenia Networks Studying Gene-Environment Interactions (EU-GEI), 2008), and now there is considerable interest in the possible synergistic effect between genes and the environment. Among environmental factors, psychosocial stress is included in most aetiological models of schizophrenia and is frequently considered a precipitating factor for psychosis in individuals with a genetic diathesis (Nuechterlein and Dawson, 1984). Family environment plays a key role in the development of psychotic symptoms, as shown by adoption studies (Tienari et al., 2004), expressed emotion research (Kavanagh, 1992; Butzlaff and Hooley, 1998) and treatment studies (Smith and Birchwood, 1987; Pitschel-Walz et al., 2001). Negative family environmental factors have been linked to poor prognosis in psychosis (Geller et al., 2000; Cooper, 2001; Myin-Germeys et al., 2001). A number of studies have noted that exposure to family members, who exhibit high levels of expressed emotion (high criticism, emotional over-involvement and negative affective style) may increase the risk of relapse in schizophrenia and bipolar disorder (Johnson et al., 1999; Johnson et al., 2003; Kim and Miklowitz, 2004; Miklowitz et al., 2004). By contrast, a positive family environment is associated with greater improvements in negative symptoms, disorganised symptoms and functioning among individuals identified as being at imminent risk of becoming psychotic (O'Brien et al., 2006). Other investigations have found that the interaction between neurocognitive vulnerability and psychosocial stress factors predicts

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psychotic thinking (Rosenfarb et al., 2000). Various environmental factors, including low socioeconomic status, are associated with a high frequency of psychotic disorders (Wicks et al., 2005; Werner et al., 2007).

Previous work has suggested that environmental and genetic influences are not independent; they may interact synergistically, augmenting the effects of each other (van Os et al., 2003; van Os et al., 2004; Heim et al., 2006; Feinberg et al., 2007; Laucht et al., 2007, van Os et al., 2008; EU-GEI, 2008). Genes can impact on a psychotic disorder indirectly by making an individual more sensitive to the psychotogenic effect of an environmental pathogen (van Os et al., 2008). On the other hand, positive environmental factors can protect vulnerable individuals against developing the disease (Feinberg et al., 2007). However, the role of protective factors has received little attention. To date, only psychosocial treatments and low doses of antipsychotics have been shown to diminish the risk of developing psychotic episodes in subjects with prodromal symptoms (Nash et al., 2004; Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines Team for the Treatment of Schizophrenia and Related Disorders., 2005; Strakowski et al., 2005). It is important to identify other potential protective factors of psychosis so that new treatments can be developed and for the primary prevention of severe mental disorders.

The study of environmental factors in early-onset syndromes seems especially important as younger people are more sensitive to positive and negative environmental factors (Ostman, 1989). This study was performed to assess if positive and negative environmental factors, together with psychotic family antecedents, are associated with the recent development of psychosis. Further, this research also investigates the interaction between genetic liability (using family history of psychosis as a proxy measure of genetic risk) and positive and negative family environment perception. Our hypothesis is that both positive and negative environmental factors are involved in the development of psychosis, and that both have a greater influence on patients with a positive family history of psychosis.

2. Method

2.1. Subjects and instruments

The sample comprised 208 subjects aged between 9 and 17 years. Of these subjects, 110 were first-episode psychotic patients recruited from child–adolescent psychiatry units at six university hospitals, and 98 were healthy controls. The patients came from six hospitals located in Madrid, Barcelona, Vitoria, Santander and Pamplona; that is, a catchment area of approximately 8 million people. This study was approved by the ethics committees of all centres involved.

The inclusion criteria for patients were: age between 7 and 17 years at the first evaluation and a first psychotic episode with positive psychotic symptoms within the previous 6 months. Patients with affective psychotic disorders such as major depressive episodes with psychotic symptoms and bipolar disorder (manic, mixed or depressive) with psychotic symptoms, and non-affective psychotic disorders such as schizophrenia spectrum diseases as defined in the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV; American Psychiatric Association, 1994), were included in the study. However, patients, who presented with a co-morbid disorder on axis I, neurological illnesses or a history of brain trauma with loss of consciousness, were excluded from the study.

The control group was selected from publicly funded schools in the community through advertisements and from individuals, who came for routine paediatric visits to hospitals in the same geographical areas as the patients. Control subjects were selected to provide a group that was proportional to the patient group regarding age, gender and socioeconomic status. Exclusion criteria for the control group were the presence of a psychiatric disorder as measured using the Kiddie-Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997), a neurological disorder, head trauma, pregnancy or mental retardation.

Family history of psychosis was evaluated using a protocol that carefully assessed first-, second- and third-degree family antecedents for mental illnesses. We determined if any of these antecedents had been diagnosed as having any psychotic disorder with delusions or hallucinations that required psychiatric treatment, according to DSM-IV criteria (American Psychiatric Association, 1994). To obtain this information, we interviewed at least one adult relative of each participant and asked them if one or several members of their family had been diagnosed with a psychotic disorder with delusions or hallucinations that required psychiatric treatment. An affirmative response placed the participant in the category FH+ (presence of Family History of psychosis), considered a proxy measure of genetic risk for psychosis, and a negative response placed them in the category FH– (absence of Family History of psychosis).

All participants completed the Family Environment Scale (FES; Moos, 1974), with the patients completing it when they were clinically stable. This scale evaluates family emotional climate according to the Camberwell Family Interview (Brown and Rutter, 1966). It has 90 true/false items evaluating the family environment in 10 different categories: COHESION (C) assesses mutual reliance; EXPRESSIVITY (EX) is the extent to which family members act freely and express their feelings directly; CONFLICTS (CON) assesses open expression of anger, aggressiveness and conflict to other members; INDEPENDENCE (IND) is the extent to which family members are sure of themselves, are independent and make their own decisions; ACHIEVEMENT ORIENTATION (AO) is the extent to which family members are achievement-orientated (such as school or work); INTELLECTUAL–CULTURAL ORIENTATION (ICO) assesses interest in political, intellectual, cultural and social issues; ACTIVE–RECREATIONAL ORIENTATION (ARO) evaluates participation in social activities; MORAL–RELIGIOUS EMPHASIS (MRE) assesses the importance given to ethical and religious practices and values; ORGANISATION (ORG) assesses the importance given at home to organisation and structure when planning the activities and responsibilities of the family; and CONTROL (CTL) is the extent to which the family abides by rules and established procedures. The 10 subscales show inter-correlations averaging around 0.20 and adequate internal consistency (Cronbach's alphas range from 0.64 to 0.79). Eight-week test–retest reliabilities ranged from 0.68 to 0.86 (Moos, 1990). The test–retest reliability of the scales in the Spanish version ranged from 0.68 to 0.86 for the 10 subscales (Moos et al., 1995). C, ICO, ARO, EX and ORG were considered as positive environmental factors, and CON, MRE, CTL, IND and AO as negative factors, in line with previous studies (Burt et al., 1988; Garcia-Camba et al., 1992; Canive et al., 1995; LeDoux et al., 1998; Thienemann et al., 1998; McGuinness et al., 2005; Vachha and Adams, 2005; Vianna et al., 2007). Global positive (FES-positive) and negative (FES-negative) family environment scores were obtained using the mean values of the respective positive and negative subscale scores.

2.2. Procedure

All participants and their parents were interviewed using the K-SADS-PL (Kaufman et al., 1997). Diagnosis was based on DSM-IV criteria (American Psychiatric Association, 1994). Those patients, who had been hospitalised during their first psychotic episode, were assessed in hospital, whereas those, who did not need hospitalisation, were contacted by their psychiatrist and assessed at outpatient facilities. The study was approved by the Institutional Review Boards of all the participating clinical centres and both parents and patients gave their written informed consent. Fifteen subjects (two controls and 13 patients) were excluded from the analyses because they had incomplete items on the FES scale or did not supply information about their family antecedents of psychosis.

2.3. Statistical analysis

The socio-demographic and clinical characteristics of the sample were described using means with standard deviations, medians with interquartile ranges or frequencies with percentages, depending on the nature of each variable. The variables were compared between patients and controls with an appropriate statistical test, namely the chi-square association test for categorical variables, the chi-square trend for proportions for ordinal variables, the non-parametric Mann–Whitney test for non-normal continuous variables and the Student's t-test when the normality assumption held.

To evaluate if each particular category of family environment in the FES has a protective effect on the risk of psychosis, one logistic regression model was fitted for each subscale of the FES for all participants (patients and controls). We used the presence of psychosis as the dependent variable, and controlled for all socio-demographic characteristics. The main effects considered were each of the FES subscales, family history of psychosis and the interaction term between the FES subscale and family history of psychosis. This allowed us to obtain the respective odds ratios (OR), to assess the joint effect of all variables adjusted for socio-demographic characteristics, and to evaluate the presence of an interaction between family environment and family history of psychosis. Finally, to summarise the information obtained, a logistic regression model was fitted with the same dependent and controlling variables, and including as main effects both the positive and negative global family environmental scales, together with family history of psychosis and the interactions between family environment and family history of psychosis. Non-significant interaction terms were removed and the final model included all controlling covariates and all significant main and interaction effects.

Statistical analyses were carried out using the free software R 2.5.1, and level $\alpha = 0.05$ was considered to determine significance.

3. Results

Table 1 summarises the descriptive characteristics of the patient and control groups. There were no significant differences between these groups in socio-demographic characteristics, except for a higher