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Demographic features and premorbid personality disorder traits in relation to age of onset and sex in paranoid schizophrenia

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ABSTRACT

Personality disorders in the premorbid period of schizophrenia and particularly in relation to age of onset and sex, seem to be a rather under-researched area. In the present study, 88 patients with paranoid schizophrenia were examined, regarding demographic characteristics and premorbid personality disorder traits, in order to investigate for differences in the premorbid period of the disease, in relation to age of onset and sex. Age cutoff points were set at < 30 years and ≥ 35 years of age for young and late onset groups, respectively. The Structured Clinical Interview for DSM-IV-Patient Edition for Axis I disorders (SCID-P) was used prospectively for diagnoses. Premorbid personality disorder traits were retrospectively assessed by using the Structured Clinical Interview for DSM-IV-Patient Edition for Axis II disorders (SCID-II). Comparisons were performed by applying the two-tailed Wilcoxon rank-sum and the χ^2 statistical tests. Young onset patients were characterized by significantly higher proportion of urban birth, single status, more avoidant premorbid personality disorder traits, and less passive-aggressive premorbid personality disorder traits, than late onset counterparts. Differences were more prominently shown in men. Earlier age of onset seems to be associated to increased social inhibition and worse psychosocial adaptation in the premorbid period of paranoid schizophrenia.

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1. Introduction

Schizophrenia is a markedly heterogeneous disorder (Tandon et al., 2008). Age of onset and sex are, among others, factors contributing to the heterogeneity of schizophrenia and, as such, there have been research efforts in order to disentangle the influence of both on the phenotype of the illness (Hafner et al., 1993).

Influence of onset age and sex on demographic features, symptoms and prognosis of patients with schizophrenia has been studied previously. Urban birth has been associated with higher risk for schizophrenia, particularly in early onset cases and males (Marcelis et al., 1998; March et al., 2008). Better psychosocial functioning and adaptation has been demonstrated in patients who get ill at an older age and in females, as can be shown by higher proportions of single persons and occupational difficulties among younger onset cases and men (Riecher-Rössler et al., 1992; Jeste et al., 1995; Hafner et al., 1999). In the active phase, most studies indicate heavier negative and disorganized symptoms in young onset cases, and heavier suspiciousness in late onset patients (Pearlson et al., 1989; Jeste et al., 1997; Palmer et al., 2001; Sato et al., 2004; Skokou et al., 2012). Although most researchers support an association of male sex with heavier negative symptoms (Mayer et al., 1993; DeLisi et al., 2001; Tang et al., 2007), it has been postulated that the above association might be due to the earlier age of onset occurring in males rather than represent a true gender effect (Skokou et al., 2012). The impact of early onset of the disorder on the symptoms of the prodromal phase has also been previously studied, and findings point to a heavier loading of negative symptoms in earlier onset cases (Hafner et al., 1998; Skokou et al., 2012). Age of onset seems to be a stronger contributor to illness heterogeneity than sex (Sato et al., 2004; Skokou et al., 2012), and therefore, needs to be taken into account when studying sex differences. However evidence regarding the relation of these parameters with premorbid personality characteristics seems to be relatively lacking.

Personality disorders of the schizophrenia spectrum, namely paranoid, schizotypal, and schizoid (Ellison et al., 1998; Nuechterlein et al., 2002) and more recently of the avoidant and dependent personality disorders (Solano and De Chavez, 2000; Fogelson et al., 2007; McMillan et al., 2009) have been reported in patients suffering from schizophrenia and/or their relatives. Avoidant personality disorder has been proposed to be included in the group of schizophrenia spectrum disorders (Fogelson et al., 2007). High scores on harm avoidance, as a temperament trait, have been consistently been reported in patients with schizophrenia (Bora and Veznedaroglu, 2007; Smith et al., 2008; Ohi et al., 2012). Patients with schizophrenia have also been shown to have higher levels of neuroticism, and lower

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levels of openness, agreeableness, extraversion and conscientiousness than healthy controls (Camisa et al., 2005), which can adversely affect coping (Lysaker and Taylor, 2007). Many of these studies have used self-report measures and mixed samples of patients with schizophrenia and schizoaffective disorder, or measure personality features after the onset of the disease.

Cutoff point for late onset schizophrenia has been put to 40 years of age, according to consensus (Howard et al., 2000); however, it has been stated that this might be too high according to epidemiological data (Beratis et al., 1994; Sham et al., 1996; Owen and Castle, 1999). A late onset group with age of onset between 35 and 60 years old has been studied in previous work (Hafner et al., 1998,1999). Other studies have used the age of 30 as a cutoff for young onset schizophrenia, by which most patients have got ill (Schultz et al., 2000; Ballageer et al., 2005). Distribution of ages of onset in paranoid schizophrenia particularly, exhibits two peaks, before the age of 30 and after the age of 35 years, the latter mostly represented by women (Beratis et al., 1994). In the present study we attempted to investigate for differences between two groups of patients, with illness onset < 30 years and ≥ 35 years, regarding demographic features and adult premorbid personality disorder symptoms, in a sample of subjects that has been also used in previous work (Skokou et al., 2012).

2. Methods

2.1. Subjects

Our study was conducted at the Department of Psychiatry of the University Hospital of Patras Medical School, which is an inpatient service admitting mostly new onset adult and adolescent cases, in an administrative area of about 1 million people. We studied 88 consecutively hospitalized patients during a three-year period, from 15 March 2005 to 7 May 2008. Patients with a diagnosis of paranoid schizophrenia, and a history of no more than three psychotic episodes were included in the study, as long as they accepted to participate. Patients who had more than three psychotic episodes were excluded from the study, so as to avoid the impact of a multi-episode course on the patients' ability to recall the premorbid period of the disorder. Patients with age of onset < 12 years and ≥ 60 years, corresponding to childhood onset schizophrenia and very late onset schizophrenia-like psychosis (Howard et al., 2000), respectively, were also excluded, as well as subjects with a history of organic brain disease or psychotic disorder due to general medical condition or substance use. Paranoid subtype was stable in the patients of the sample throughout the course of their illness, which is not surprising, since this is the subtype with the greater stability among all subtypes of schizophrenia (Kendler et al., 1985).

Age of onset was defined as the age at which the first prodromal symptom was demonstrated. Cutoff points for the comparison groups were set at 30 years of age, referred to as young onset group (range: 12–29 years) ($N=60$), and 35 years of age (range: 35–57 years) ($N=21$), as late onset group, in the present work. A group of seven patients had disease onset between 30 and 35 years of age; this was not further examined due to its very small size.

After complete description of the study to the subjects, written informed consent was obtained. The study was approved by the ethics and deontology committee of the University Hospital of Patras.

2.2. Procedures

The diagnosis of schizophrenia, paranoid type, was made prospectively, during the patients' hospitalization, by the author MS, according to Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) (American Psychiatric Association, 2000), using the structured clinical interview for DSM-IV-Patient Edition for Axis I disorders (SCID-P) (First et al., 1995). Patients were interviewed regarding their birth place, residence place, marital status and educational status.

After remission of the active psychotic phase, the patients were retrospectively assessed for adult premorbid personality disorder traits by applying the structured clinical interview for DSM-IV-Patient Edition for Axis II disorders (SCID-II) (First et al., 1997), for patients who demonstrated their first initial prodromal symptom after the age of 18, with additional information obtained by their family members. The patients were frequently reminded during the interview to answer the questions based on how they felt and behaved during the premorbid period of their illness. Remission was clinically tested according to the symptom-based criterion of symptomatic remission (Andreasen et al., 2005), corresponding to a score ≤ 3 on eight diagnostically relevant symptoms of the Positive and Negative

Syndrome Scale (PANSS), namely delusions, unusual thought content, hallucinatory behavior, conceptual disorganization, mannerisms/posturing, blunted affect, passive/apathetic social withdrawal, as well as lack of spontaneity and flow of conversation. Absence of manifestations other than mild ones was considered important, so that serious positive or negative symptoms would not substantially interfere with the interview and the recall process. The SCID II can be used for categorical and/or dimensional assessment of 12 personality disorders, namely paranoid, schizoid, schizotypal, comprising cluster A, histrionic, narcissistic, borderline, antisocial, comprising cluster B, avoidant, dependent, obsessive-compulsive, comprising cluster C personality disorders, and passive-aggressive and depressive personality disorders. Traits of personality disorders correspond to the items of the SCID II, which represent the DSM-IV-TR criteria (symptoms) of each of the 12 personality disorders assessed by this instrument, and are rated (1) (absent), (2) (subthreshold), and (3) (present). A rating of (3) is necessary to diagnose a personality disorder trait. The SCID II was not applied to patients who became ill before the age of 18, because in these cases it would not have been possible to distinguish reliably between prodromal or active phase symptoms and premorbid personality disorder symptoms. The prodromal symptoms assessed were those listed in DSM-III-R (American Psychiatric Association, 1987) as elaborated previously (Gourzis et al., 2002), and were obtained by applying the structured clinical interview for DSM-III-R, Patient Edition (Spitzer et al., 1990) and clinical interviewing for additional symptoms of each patient and at least one of significant others (Skokou et al., 2012). A sensitivity analysis regarding premorbid personality disorder traits was also conducted, using consensus age cutoff points, < 40 for young onset and ≥ 40 years for late onset groups.

2.3. Statistical analysis

A non-parametric statistical test for unpaired data (two-tailed Wilcoxon rank-sum test) was used for comparing differences between the groups for the number of premorbid personality disorder traits studied. The χ^2 statistical test was used for comparing differences between the groups for the demographic features studied.

Comparisons were made between the young onset and late onset groups, separately for male and female patients (young onset vs. late onset), and also between the two sexes (male vs. female patients), within each age-of-onset group. Differences were considered statistically significant if p-values were lower than 0.05.

Statistical analysis was performed, using a statistical software package tool (NCSS Statistical software 2007, Kaysville, Utah, USA).

2.4. Inter-rater reliability

In order to assess inter-rater agreement, 20 of the patients were re-evaluated by applying SCID-P and SCID-II, by another staff psychiatrist, who was unaware of the results of the evaluation of the previous interviewer. The inter-rater agreement between the two examiners was studied by means of the unweighted *kappa (k)* statistical test. There was complete agreement between the two diagnosticians for the diagnosis of paranoid schizophrenia ($k=1.0$). Inter-rater reliability for each item of the SCID-II was substantial to perfect, with $0.64 \leq k \leq 1.0$. In all cases, the agreement observed was statistically significant ($0.00001 < p < 0.048$).

3. Results

3.1. Number of episodes, age and age of onset

The number of psychotic episodes was not significantly different among the groups studied. Of young onset males ($N=46$), 25 (54%) were in their first, 15 (33%) were in their second and 6 (13%) were in their third psychotic episode, compared with 5(63%), 2(25%) and 1(13%) of late onset males ($N=8$), respectively. Regarding females, the number of patients in their first, second, or third psychotic episode were 6(43%), 5(36%), 3(21%) and 8(62%), 4(31%), 1(8%) for the young onset ($N=14$) and late onset group ($N=13$), respectively.

The mean age $\pm$ standard deviation (S.D.) of the patients at admission was 30.7 ± 8.7, with a range from 17 to 59 years for males, and 36.5 ± 10.6, with a range from 21 to 65 years for females (Table 1). Young onset females become ill on average 3 years later than young onset males ($z=2.14$, $p=0.032$). The age of onset in the late onset group is not significantly different between the two sexes ($z= -0.59$, $p=0.558$) (Table 1).