



Cognitive profiles of three clusters of patients with a first-episode psychosis

Susana Ochoa^{a,*}, Elena Huerta-Ramos^{a,c}, Ana Barajas^{a,b,c,d}, Raquel Iniesta^{a,c}, Montserrat Dolz^b, Iris Baños^{a,c}, Bernardo Sánchez^b, Janina Carlson^{a,b,c}, Alexandrina Foix^a, Trinidad Pelaez^a, Marta Coromina^a, Marta Pardo^b, the GENIPE group¹, Judith Usall^a

^a Parc Sanitari Sant Joan de Déu. Sant Boi de Llobregat (Barcelona), CIBERSAM, Spain

^b Hospital Infanto-juvenil Sant Joan de Déu. Esplugues de Llobregat (Barcelona), CIBERSAM, Spain

^c Fundació Sant Joan de Déu. Esplugues de Llobregat (Barcelona), CIBERSAM, Spain

^d Centro de Higiene Mental de Les Corts (Barcelona), Spain

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ABSTRACT

Objective: The primary objective was to identify specific groups of patients with a first-episode psychosis based on family history, obstetric complications, neurological soft signs, and premorbid functioning. The secondary objective was to relate these groups with cognitive variables.

Method: A total of 62 first-episode psychoses were recruited from adult and child and adolescent mental health services. The inclusion criteria were patients between 7 and 65 years old (real range of the samples was 13–35 years old), two or more psychotic symptoms and less than one year from the onset of the symptoms. Premorbid functioning (PAS), soft signs (NES), obstetric complications and a neuropsychological battery (CPT, TMTA/TMTB, TAVEC/TAVECI, Stroop, specific subtest of WAIS-III/WISC-IV) were administered.

Results: We found three clusters: 1) higher neurodevelopment contribution ($N = 14$), 2) higher genetic contribution ($N = 30$), and 3) lower neurodevelopment contribution ($N = 18$). Statistical differences were found between groups in TMTB, learning curve of the TAVEC, digits of the WAIS and premorbid estimated IQ, the cluster 1 being the most impaired.

Conclusions: A cluster approach could differentiate several groups of patients with different cognitive performance. Neuropsychological interventions, as cognitive remediation, should be addressed specifically to patients with more impaired results.

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1. Introduction

In recent years an increasing interest in the assessment of cognitive variables in people with schizophrenia and first-episode psychosis has emerged. The results of most of the studies carried out have demonstrated a neurocognitive deficit in people with schizophrenia and first-episode psychosis. The most prevalent cognitive impairments detected

in people with schizophrenia are those related to deficits of memory, executive function and attention (Green, 1996; Hoff and Kremen, 2003; Sharma and Antonova, 2003; Dickinson et al., 2007; Nuechterlein et al., 2008; Brébion et al., 2012).

Memory and learning problems were among the most studied cognitive variable in first-episode psychosis related to control groups, showing a worse functioning in people with a first-episode psychosis (Bilder et al., 2000; Galderisi et al., 2009; Zanello et al., 2009; Holmén et al., 2010; Jahshan et al., 2010; Zabala et al., 2010). O'Connor et al. (2009) point out that verbal memory is affected in people with a first episode psychosis regardless of the premorbid IQ. Moreover, Galderisi et al. (2009) found that people with a first episode psychosis scored worse than healthy controls in processing speed, motor dexterity, and cognitive flexibility tasks. Zabala et al. (2010), in a sample of early-onset first-episode psychosis, add attention to this list.

However, not all people with a first-episode psychosis performed worse than controls in cognitive assessment (Leeson et al., 2010; Bartholomeusz et al., 2011). Some of this variability may be explained by the presence of latent subgroups that differ in etiology and key neurobiological underpinnings. Identifying these subgroups could help

* Corresponding author at: Research and Development Unit of Parc Sanitari Sant Joan de Déu, CIBERSAM, Edifici Sant Rafael, primera planta C/Dr. Pujades, 42, Sant Boi de Llobregat, Barcelona, Spain. Tel.: +34 936406350x12538.

E-mail address: sochoa@pssjd.org (S. Ochoa).

¹ The GENIPE group is a multidisciplinary group of researchers that includes Araya S, Arranz B, Arteaga M, Asensio R, Autonell J, Baños I, Bañuelos M, Barajas A, Barceló M, Blanc M, Borrás M, Busquets E, Carlson J, Carral V, Castro M, Corbacho C, Coromina M, Dachs I, Dolz M, Domenech MD, Elias M, Espezel I, Falo E, Fargas A, Foix A, Fusté M, Godrid M, Gómez D, González O, Granell L, Gumà L, Haro JM, Herrera S, Huerta E, Lacasa F, Mas N, Martí L, Martínez R, Matalí J, Miñambres A, Miquel L, Muñoz D, Muñoz V, Nogueroles R, Ochoa S, Ortiz J, Pardo M, Planella M, Pelaez T, Peruzzi S, Rivero S, Rodriguez MJ, Rubio E, Sammut S, Sánchez M, Sánchez B, Serrano E, Solís C, Stephanotto C, Tabuenca P, Teba S, Torres A, Urbano D, Usall J, Vilaplana M, and Villalta V.

to improve the treatment of schizophrenia and first-episode psychosis (Jindal et al., 2005).

According to the neurodevelopment hypothesis, the etiology of psychosis may involve pathological processes, caused by both genetic and environmental factors that begin before the brain approaches its adult anatomical state in adolescence (Fatemi and Folsom, 2009). Several markers of congenital alterations indicative of neurodevelopmental insults have been found. It is well documented that there are higher rates of neurological soft signs in patients with schizophrenia than in healthy controls (Heinrichs and Buchanan, 1988); moreover this higher prevalence has been observed in first-episode patients (Bombin et al., 2005; Compton et al., 2007; Ruiz-Veguilla et al., 2008; Mayoral et al., 2012). In addition, there is consistent evidence showing that a large number of people affected by the spectrum of psychotic disorders manifest poor social and academic adjustment prior to initiation of the disease (Allen et al., 2001; Norman et al., 2005; Monte et al., 2008).

Emerging evidence points to schizophrenia as a familial disorder with a complex mode of inheritance and variable expression (Meltzer and Fatemi, 2000). Moreover, Gottesman et al. (2010) found a higher familial risk when one or two parents presented a mental disorder. The study also differentiated a higher risk in the offspring of couples diagnosed with a psychiatric disorder than in children with only one affected parent. While familial risk factors account for a significant rate of predisposition to schizophrenia, there is also evidence of an important environmental contribution. Obstetric complications are among the most studied environmental indicators of risk for schizophrenia (Clarke et al., 2006).

All the variables described above are associated with schizophrenia and psychotic disorders and can be detected prior to onset of symptoms. They may, in part, help us to explain the heterogeneity of spectrum of psychotic disorders. To explore this we chose to use an approach based on cluster analysis. K-means clustering has been used to examine the heterogeneity of psychotic disorders (Lee et al., 2011; Dawes et al., 2011; Ruiz-Veguilla et al., 2008; Richards et al., 2008). However, no previous studies have used cluster analysis either for grouping patients according to factors prior to onset of illness or for grouping patients in samples of first-episode of psychosis.

1.1. Aims of the study

Our study investigated a group with a first-episode psychosis to explore whether specific groups of patients can be identified on the basis of family history risk, obstetric complications, neurological soft signs, and premorbid functioning. The second step of the study was to examine the relationship of these groups of patients to cognitive variables.

2. Material and methods

2.1. Subjects

The sample was comprised of 62 consecutive patients with a first-episode psychosis. The patients were recruited from adult mental health services and from the child and adolescent mental health services at *Sant Joan de Déu*, both from hospital and community psychiatric services. These centers cover the Barcelona city and metropolitan areas.

The inclusion criteria were: two or more psychotic symptoms (criteria A DSM-V); age between 7 and 65 years; less than 6 months since the first contact with the medical service; and less than a year since development of symptoms. Patients diagnosed with intellectual disabilities (premorbid IQ < 70) or head injury were excluded from the study.

All selected individuals were informed of the study objectives and methodology by their psychiatrist and signed the required informed consent form. In the case of children and adolescents, informed consent

was obtained from parents and from the service users themselves. The study was approved by the *Sant Joan de Déu* Independent Ethics Committee.

In terms of sociodemographic characteristics, 35 patients were male (56.5%), 60 were single (96.8%), 59 were living with their parents (95.2%), 32 were studying (52.5%), 9 were working (14.8%), 12 were unemployed (19.7%) and 6 were on sick leave (9.8%). Mean age was 19 years old ($DS = 5.2$). The age range of the sample was between 13 and 35 years old.

The patients had been diagnosed as follows: 15 with non-specified psychotic disorder (24.2%); 17 with schizophreniform disorder (27.4%); 10 with bipolar disorder (16.1%); 8 with major depression (12.9%); 6 with schizophrenia (9.7%); 2 with delusional disorder (3.2%); 2 with brief psychotic disorder (3.2%); 1 with schizoaffective disorder (1.6%); and 1 with drug-induced psychosis (1.6%).

2.2. Instruments

The assessment was performed by two trained psychologists. The evaluators scored over 0.70 in the intraclass correlation coefficient of the instruments before the start of the study.

The socio-demographic characteristics and clinical variables of the sample were assessed through a questionnaire.

The following scales were used for the variables in the cluster analysis:

- The Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982; Barajas et al., 2013): a 26-item scale, which evaluates sociability and withdrawal, social relationships, adaptation to and behavior at school in: childhood, early adolescence, late adolescence, and adulthood, as well as social-sexual aspects from early adolescence. The total PAS scores were in the range of 0.0 to 1.0, where higher scores represented lower levels of premorbid adjustment. The academic and social subscales of premorbid function were used (Norman et al., 2005).
- The Neurological Evaluation Scale (NES) (Buchanan and Heinrichs, 1989): a 26-item scale for assessing soft signs. Higher rates in total score show greater presence of neurological soft signs.
- The obstetric complication scale by Lewis and Murray (1987) was administered to the patients' mother in order to assess the presence obstetric complications (Geddes et al., 1999). Higher scores indicated more obstetric complications.
- Finally, family history was assessed by determining the presence of mental health disorder in first-degree relatives (only parents) through the Family History-RDC interview (Andreasen et al., 1977). The variable included in the analysis was the sum of family history of mental disorder of the two parents.

Neuropsychological performance was assessed by a battery of tests. The scores used in the analyses were demographically-adjusted (t distribution) according to the Spanish validation of the instruments.

- The Continuous Performance Test (CPT) (Conners, 2002) was used to assess inhibition, attention capacity and processing speed. The variables included were errors in omissions and commissions, and the processing speed index.
- The Trail Making Test (TMT) A and B (Reitan and Wolfson, 1995) allowed us to assess attention capacity, cognitive flexibility, and visual-motor speed.
- The Wechsler Adult Intelligence Scale (WAIS) (Seisdedos et al., 1999) and the Wechsler Intelligence Scale for Children (WISC), Spanish version (Corral et al., 2005), were used to assess intelligence. WAIS was used for people aged over 16 and WISC for children and adolescents under 16. The subscales used in our study were vocabulary, arithmetic, digits and numbers. The estimated IQ was calculated by vocabulary subtest as suggested previously by several authors (Mirallbell et al., 2010).

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