



Premorbid adjustment and clinical correlates of cognitive impairment in first-episode psychosis. The PEPsCog Study



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ABSTRACT

Background: The extent to which socio-demographic, clinical, and premorbid adjustment variables contribute to cognitive deficits in first-episode schizophrenia spectrum disorders remains to be ascertained.

Aims: To examine the pattern and magnitude of cognitive impairment in first-episode psychosis patients, the profile of impairment across psychosis subtypes and the associations with premorbid adjustment.

Methods: 226 first-episode psychosis patients and 225 healthy controls were assessed in the PEPsCog study, as part of the PEPs study.

Results: Patients showed slight to moderate cognitive impairment, verbal memory being the domain most impaired compared to controls. Broad affective spectrum patients had better premorbid IQ and outperformed the schizophrenia and other psychosis groups in executive function, and had better global cognitive function than the schizophrenia group. Adolescent premorbid adjustment together with age, gender, parental socio-economic status, and mean daily antipsychotic doses were the factors that best explained patients' cognitive performance. General and adolescent premorbid adjustment, age and parental socio-economic status were the best predictors of cognitive performance in controls.

Conclusions: Poorer premorbid adjustment together with socio-demographic factors and higher daily antipsychotic doses were related to a generalized cognitive impairment and to a lower premorbid intellectual reserve, suggesting that neurodevelopmental impairment was present before illness onset.

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¹ Information about PEPs Group is available in Appendix A.

1. Introduction

Cognitive deficits are considered core features of schizophrenia spectrum disorders and, among other reasons, they are considered important for their impact on functional outcome (Green et al., 2004). FEP represents an excellent opportunity for research, because confounding factors such as hospitalization, long-term treatments and chronicity are minimized (Goldberg et al., 2010).

The cognitive profile of schizophrenia patients has been widely detailed in research, presenting a generalized cognitive impairment and specific deficits in attention, memory and learning, executive functions, working memory and processing speed (Heinrichs and Zakzanis, 1998; Flashman and Green, 2004; Reichenberg and Harvey, 2007). Regarding other psychotic disorders, research has focused primarily on the comparison between schizophrenia and psychotic affective disorders, reporting milder deficits in bipolar patients although qualitatively similar to patients with schizophrenia (Schretlen et al., 2007; Reichenberg et al., 2009; Aas et al., 2014). Schizophrenic patients also show greater effect sizes in premorbid and current intelligence quotient (IQ) at illness onset when compared to other psychosis (Zanelli et al., 2010).

Several premorbid factors, such as a lower IQ and poorer adjustment, have been associated with cognitive impairment in the early phases of psychosis. However, there is no agreement on these findings. Otherwise, premorbid IQ (van Winkel et al., 2006) as well as IQ at psychosis onset (Leeson et al., 2009; Leeson et al., 2010) have been shown to be predictors of functional outcome in the long term. These findings support the cognitive reserve theories (Barnett et al., 2006), which propose that patients with higher premorbid intellectual function have more resilience to cope with the neural damage associated with the illness, better brain structure or neural functionality compensating for the deficits.

Premorbid adjustment refers to a subject's social, interpersonal, academic and occupational functioning prior to the onset of psychotic symptoms (Addington and Addington, 2005). Poor premorbid adjustment has been related to higher rates of relapse and poorer clinical outcome (Addington and Addington, 2005; Levy et al., 2012). Neurodevelopmental disturbances are assumed to underlie poor premorbid adjustment, which represents one of the key prognostic indicators of schizophrenia (McGlashan, 2008). The relationship between premorbid adjustment and cognitive functioning has been examined in several studies. In a sample of FEP, Rund et al. (2007) found that a good premorbid level of academic functioning was associated with better verbal learning outcomes 1 year after the episode and better working memory outcomes 2 years later. A strong association has been found between poor childhood academic functioning and poor outcomes on working memory tests (Larsen et al., 2004).

The "Phenotype-genotype and environmental interaction. Application of a predictive model in first psychotic episodes" or PEPs study is a multicentre, longitudinal, naturalistic, follow-up study designed to evaluate clinical, neuropsychological, neuroimaging, biochemical and genetic variables in a sample of 335 first-episode psychosis (FEP) patients in Spain, matched with healthy controls by age, sex and socio-economic status. Patients were recruited from sixteen centers located across Spain from April 2009 to April 2011. The aim of this project was to assess clinical characteristics, functional prognostic factors, diagnostic specificity of findings, and pathophysiological changes in the brain during the first 2 years after a first psychotic episode (Bernardo et al., 2013).

The aims of the present study were to examine: 1) the pattern and magnitude of cognitive impairment in FEP patients after clinical stabilization of the acute episode; 2) the differences between psychosis subtypes and healthy control groups; 3) the relationship between premorbid adjustment abnormalities with cognitive impairment; and 4) the relative contribution of premorbid adjustment abnormalities to cognitive impairment taking account of the main socio-demographic and clinical variables.

2. Methods

The PEPs study was composed of four modules: general, pharmacogenetics, neuroimaging and neurocognition. In the current article, we focus on the neurocognition module (hereon referred to as the PEPsCog study), so the data presented concern the participants who were included in this module.

2.1. Participants

The patients included in the PEPs study met the following inclusion criteria: age between 7 and 35 years old, presence of psychotic symptoms of less than 12 months' duration, being fluent in Spanish and provision of written informed consent. The exclusion criteria were: mental retardation according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (APA, 1994) criteria (including both an IQ below 70 and impaired functioning), history of head trauma with loss of consciousness and organic disease with mental repercussions. The healthy control subjects were matched with the patients according to their age ($\pm 10\%$) and the socio-economic status (SES) of their parents ± 1 level (see below). Controls also had to be fluent in Spanish and give a written informed consent. The exclusion criteria for controls were the same as for the patients, plus the presence of a present or past psychotic disorder or major depression. The study was approved by the research ethics committees of all participating clinical centers.

In the PEPs study, the patients were assessed on five occasions: at recruitment (baseline), and then at two months, six months, one year and two years. Controls were only assessed at baseline and two years. The patients' cognitive assessments were performed at the two-month visit to ensure their clinical stability. The current report is based on premorbid, clinical and cognitive data gathered at baseline and two months.

Initially, 335 FEP patients and 253 controls were included in the PEPs study. The PEPsCog study included the participants who completed more than one neuropsychological test ($n = 547$; 515 adults and 32 under 16 years old participants). For the purposes of the present study, we only included the adult participants who completed seven or more of the ten neuropsychological tests of the study, which represented more than 95% of the sample. The final sample for the PEPsCog study consisted of 491 subjects: 266 patients and 225 controls.

2.2. Procedures

2.2.1. Clinical assessments

Demographic and premorbid data were collected for all participants, including age, gender, years of education, current occupation and living arrangements. Parental socio-economic status (SES) was assessed with the Hollingshead-Redlich Index of Social Position (Hollingshead and Redlich, 1958).

Psychopathological assessment was carried out with the Positive and Negative Symptom Scale (PANSS; Kay et al., 1987; Peralta and Cuesta, 1994), the Young Mania Rating Scale (YMRS; Young et al., 1978) and the Montgomery-Asberg Depression Rating Scale (MADRS; Lobo et al., 2002; Montgomery and Asberg, 1979).

Pharmacological treatment was also recollected at each visit. Antipsychotic daily doses were converted to chlorpromazine equivalents (Gardner et al., 2010).

Diagnoses were determined with the SCID-I and II (First et al., 1997a, 1997b) according to the DSM-IV criteria. Then the patients were grouped into three diagnostic categories: 1) broad schizophrenia spectrum (BS) patients, which included schizophrenia, schizophreniform and schizoaffective disorders; 2) broad affective spectrum (BA) patients, which included bipolar disorder I and II, and manic and depressive episodes with psychotic symptoms; and 3) other psychoses

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