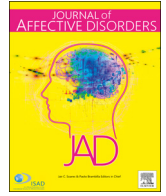




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Research paper

Affective versus first-episode non-affective first-episode psychoses: A longitudinal study



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ABSTRACT

Objective: This study aimed to assess (1) whether there were clinical, neuropsychological and functional differences between and within affective and non-affective psychoses at baseline and two years-follow-up and (2) to explore clinical and neuropsychological predictors of psychosocial functioning in the whole sample.

Method: This is a subanalysis from a multicentre, naturalistic, longitudinal prospective study ('Phenotype-genotype and environmental interaction. Application of a predictive model in first psychotic episodes'). The sample consisted of 192 patients with a first psychotic episode (FEP): 142 with non-affective psychoses and 50 with affective psychoses. Student *t*-tests, paired *t*-tests, Pearson correlations, ANOVAs and regression analyses were performed.

Results: At baseline, the groups differed in perseverative errors (WCST), Premorbid Adjustment Scale (PAS), family history of psychiatric disorder, negative (PANSS) and manic symptoms (YMRS). At two years follow-up, the groups differed in all the PANSS subscales and in depressive symptoms assessed by the MADRS. When the whole sample was considered, the regression model which best explained the estimated variance in functioning at follow-up (41%) was composed by PANSS total score and verbal fluency assessed by the FAS (COWAT).

Conclusions: We found clinical and neurocognitive differences at baseline which decreased in the follow-up. Reduced performances at baseline in executive functions in combination with symptom severity (PANSS) were predictors of FEP patients' poor functional outcome.

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1. Introduction

There is increasing evidence for clinical, cognitive, neurophysiological and genetic overlap between bipolar disorder and schizophrenia (Arrasate et al., 2016a; Knochel et al., 2016; Schaefer et al., 2013) suggesting the existence of a psychoses spectrum (Arrasate et al., 2014; Craddock and Owen, 2010). In particular, cognitive problems are a highly relevant dimension across different psychiatric conditions; the impairment may vary quantitatively depending on the severity and characteristics of the underlying illness (Millan et al., 2012). Several studies found similar cognitive patterns between schizophrenia and bipolar disorders with quantitative rather than qualitative differences between the diagnostic groups, being the group with schizophrenia, quantitatively, more affected (Stefanopoulou et al., 2009; Yen et al., 2009). Moreover, in prospective studies, it has been suggested that schizophrenic and bipolar patients are distinguished by premorbid cognitive impairment being found in the former but not the latter (Cuesta et al., 2015a; Lewandowski et al., 2011). Following the illness onset, both disorders seem to be associated with further cognitive impairment, which is of greater magnitude in schizophrenia than bipolar disorder (Trotta et al., 2015). Likewise, with repeated episodes of illness brain structural abnormalities accumulate in both schizophrenia and bipolar disorder (Arango et al., 2012; Demjaha et al., 2012; Hibar et al., 2017; Rosa et al., 2012). In the last years, the identification of biomarkers in cognition has been the focus of the research in schizophrenia and bipolar disorder, some of the studied aspects are: the relationship between inflammation and cognition and the association of cognition and neurotrophic factors (Penades et al., 2015). The identification of biomarkers as measures of pathophysiological processes could provide meaningful targets for the development of new and personalised treatments.

Birth cohort and conscript studies report strong associations between poor performance on cognitive batteries and increased risk of later schizophrenia (MacCabe et al., 2008). It seems that cognitive development is abnormal in children and adolescents who will develop schizophrenia (Bora, 2015). A systematic review and meta-analysis confirmed the presence of a premorbid IQ deficit deviations among young people who will later develop schizophrenia (Woodberry et al., 2008). In contrast to findings in schizophrenia, premorbid deficits in bipolar disorder seem to be absent or even reversed (Grande et al., 2016). Kumar and Frangou (Kumar et al., 2010) found normal or superior cognitive abilities and school achievement in children and adolescents who develop adult bipolar.

Neurodevelopmental cognitive impairment is evident in some but not all patients with bipolar disorder (Bora, 2015), as a case in point neurological soft signs might be more common in bipolar disorder than in healthy controls (Zhao et al., 2013). Little is known about the relationship between cognitive dysfunctions and the structural and functional brain abnormalities that characterise bipolar disorder. Processing and regulation negative emotions (Sepede et al., 2015) and sustained attention have been suggested as a potential trait marker in bipolar I disorder Sepede et al. (2015). During a negative emotion task, euthymic bipolar I patients and non-affected first-degree relatives shared an abnormal activation of a limbic area and a reduced activation of a parietal region (Sepede et al., 2012).

Moreover some studies suggested that cognitive impairment in bipolar disorder could be associated with abnormalities in genes that have a role in brain development (Tabares-Seisdedos et al., 2008). This is also the case for schizophrenia (Howes and Murray, 2014).

Cognitive impairment has significant implications for long-term functional outcomes in these disorders, as demonstrated by, reduced rates of employment and independent living, lacking reliable friends and leisure activities independent of clinical symptomatology (Depp et al., 2012). In both disorders, executive function is together with social cognition the most commonly reported neurocognitive domains to be related with psychosocial functioning. Studies on social

cognition report deficits in emotion recognition and theory of mind in schizophrenic populations (Bora et al., 2009; Kohler et al., 2010), a meta-analysis even reported that social cognition maybe more promising than non-social neurocognition in predicting functionality in schizophrenia (Fett et al., 2011). The presence of some cognitive deficits in FEP patients has been associated also with negative symptoms (Gonzalez-Ortega et al., 2013). The studies on first episode psychotic patients are of a great interest in order to better characterize this sub-population avoiding the effects of chronicity and to determine functional prognosis.

To clarify the cognitive trajectory of schizophrenia and bipolar disorders and which variables would be the best predictors of psychosocial functioning, we have followed-up a sample of first psychotic episodes. The aims of the current study were (1) to assess whether there were clinical, neuropsychological and functional differences between and within affective and non-affective psychoses at baseline and two years-follow-up (2) to explore clinical and neuropsychological predictors of psychosocial functioning in the whole sample.

2. Methods

This work is part of the study: ‘Phenotype-genotype and environmental interaction. Application of a predictive model in first psychotic episodes’ or PEPS study. It is a multicentre, longitudinal, naturalistic follow-up study composed of four modules: general, pharmacogenetics, neuroimaging and neurocognition (Bernardo et al., 2013). The current study was focused on the general and neurocognition modules (Cuesta et al., 2015a).

2.1. Participants

The 16 Spanish centers participating in the PEPs project recruited a total of 335 patients with a first episode psychosis (FEP) and 253 healthy controls from April 2009 to April 2011. Fourteen of these expert centers are integrated in the well-recognized Spanish network for research on mental disorders, the Center for Biomedical Research Network on Mental Health (Centro de Investigación Biomédica en Red de Salud Mental, CIBERSAM), which has a broad experience in research and clinical management. The patients were recruited from the inpatient or outpatient settings of the 16 centers. The diagnostic evaluation was performed with a very comprehensive protocol with strict inclusion and exclusion criteria making this sample well-defined and representative to be as close as possible to the population with a FEP. Moreover, this is a multi-centre study that includes a large sample of patients and controls recruited in multiple Spanish psychiatric admission centres for acute psychosis, ensuring the generalizability of the results.

Patients who met the inclusion criteria that were attended at these facilities during the recruitment period were invited to participate in the study. The inclusion criteria of the study were: (1) age between 7 and 35 years old (2) presence of psychotic symptoms of less than 12 months’ duration (3) being fluent in Spanish and (4) provision of written informed consent.

The exclusion criteria were: (1) mental retardation according to the Diagnostic and Statistical Mental Disorders, Fourth Edition (APA, 1994) criteria (including both and IQ below 70 and impaired functioning), (2) history of head trauma with loss of consciousness and (3) presence of organic disease gathered by clinical interview and completed with clinical records. The research ethics committees of all participating clinical centers approved the study. Written informed consent was obtained from all participants. In case of children under 18 years of age, patients assented to participate and parents or legal guardians gave written informed consent before their inclusion.

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 at two years.

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