



Neuropsychological characteristics of child and adolescent offspring of patients with bipolar disorder



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ABSTRACT

Background: Bipolar disorder (BD) is a severe mental disorder with a strong genetic component. The assessment of child and adolescent offspring of patients diagnosed with BD (BDoff) provides an opportunity to investigate vulnerability factors and the first abnormalities associated with the disorder. Previous literature in child and adolescent BDoff is scarce and controversial. However, some studies concur in identifying significant impairment in executive functions, memory and attention. The present study aims to compare global neuropsychological characteristics of child and adolescent offspring of patients with bipolar disorder with a group of offspring of parents with no history of psychotic disorder, and to assess the influence of psychopathology on neuropsychological performance.

Methods: This research was part of The Bipolar and Schizophrenia Young Offspring Study (BASYS). A group of BDoff (N = 90) and a group of offspring of parents with no history of psychotic disorder (CC) (N = 107) were assessed with a complete neuropsychological battery. Intellectual quotient, working memory, processing speed, verbal memory and learning, visual memory, attention and executive functions were included in the cognitive assessment.

Results: BDoff showed significantly worse performance in processing speed and immediate recall of visual memory relative to CC. When the presence of any lifetime psychopathology was analysed, the results showed that belonging to the BDoff group was the main explicative factor for the scores obtained in both processing speed and visual memory immediate recall, regardless of the presence of psychopathology.

Conclusions: These findings suggest that processing speed and visual memory should be taken into consideration in future research on vulnerability markers of BD.

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1. Introduction

Bipolar disorder (BD) is a severe mental disorder affecting between 0.6–2.4% of the general population (Merikangas et al., 2011) and 1.2% of

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children and adolescents (Kessler et al., 1994). The heritability of the disorder has been estimated between 56 and 93% (McGuffin et al., 2003; Kiesseppa et al., 2004; Lichtenstein et al., 2009), and the genetic component has been considered one of the most important risk factors for developing the disorder (McGuffin et al., 2003; Jones and Bentall, 2008). The risk of BD in offspring of patients is about 4 to 5% when one parent is affected, increasing to 14–35.8% if both parents are diagnosed with BD (Chang et al., 2003; Wray and Gottesman, 2012). Therefore, the assessment of child and adolescent offspring of patients diagnosed with BD (BDoff) provides the opportunity to investigate the first abnormalities and vulnerability factors for the illness in a sample at increased risk for the disorder (Duffy et al., 2000; DelBello and Geller, 2001).

Cognitive deficits in both adult and child patients with BD have been widely documented. The most consistent findings reported in adult

samples have been difficulties in verbal memory, attention and executive functions (Torres et al., 2007; Lim et al., 2013). Moreover, these difficulties have been identified in all stages (acute, euthymic and chronic) of the illness (Clark et al., 2002; Martinez-Aran et al., 2004; Balanza-Martinez et al., 2005). In children and adolescents diagnosed with BD, the literature suggests a similar pattern of cognitive impairments to the one observed in adult populations. Deficits in verbal memory, attention and executive functions are the most commonly reported neuropsychological abnormalities (Cahill et al., 2009; Horn et al., 2011).

With regard to previous literature concerning first degree relatives of patients diagnosed with BD, studies performed with adult populations have shown overall similar cognitive deficits as those observed in BD patients, but less severe. Specifically, Balanza-Martinez et al. (2008) who systematically reviewed 23 studies, mainly conducted in adult samples, found that 54% of them reported impairments in verbal learning and memory, 33% in working memory, 25% in attention and executive functions and 20% in processing speed. Nevertheless, only 12.5% of the studies found lower scores in intelligence tests in first degree relatives than in controls.

Turning to child and adolescent samples, Doyle et al. (2009) conducted a study comparing neuropsychological performance of 170 youths with BD, 118 non mood-disordered siblings and 79 non mood-disordered controls. They found significant differences between the sibling group and the control group in the problem-solving factor and in working memory, both of which are associated with executive functions.

With regard to studies performed with child and adolescent BDoff, McDonough-Ryan et al. (2002) compared the general intellectual functioning and the academic achievement of a group of 28 BDoff children (mean age 10.2) and 24 healthy controls (mean age 10) whose parents were free of psychopathology. The authors did not find any differences between groups in terms of verbal, performance or full scale IQ. They did, however, observe a significantly higher rate of discrepancy between verbal and performance IQ in the BDoff group.

In another study, Diwadkar et al. (2011) assessed working memory and attention in a sample of BDoff (N = 23) with a mean age of 14.5, a group of schizophrenia offspring (N = 36) with a mean age of 14 and a group of healthy controls, offspring of parents with no history of psychosis in first degree relatives (N = 41), with a mean age of 14.9. Due to the high rate of attention deficit hyperactivity disorder (ADHD) observed in the schizophrenia and bipolar offspring groups, the authors included the presence of ADHD as covariate in the statistical analysis. The results showed that the schizophrenia offspring had worse performance in working memory, while the BDoff showed significantly lower scores in attention, both compared to HC group.

To our knowledge, only one study so far undertaken in adolescent BDoff has included a comprehensive neuropsychological battery evaluating a range of cognitive functions (Klimes-Dougan et al., 2006). In this study, the authors assessed a sample of offspring of mothers with major depressive disorder (MDDoff, N = 72), 43 BDoff and 50 community controls, with parents free of any axis I disorder. The mean age of the three groups ranged between 15.1 and 16 years. The results showed that the BDoff group had lower scores than the control group in IQ, executive functions, spatial memory and attention. Most of these results remained stable after controlling for depressive and manic symptoms. No significant differences were found between the MDDoff and controls in any cognitive area.

As can be inferred from the above literature, cognitive studies conducted specifically in child and adolescent BDoff are scarce. The majority of them have assessed only some cognitive areas, and as a result it is difficult to obtain a complete picture of the neuropsychological difficulties which characterise BDoff. Moreover, in many cases, the small sample size, the inclusion of healthy controls (with no axis I disorders) and the lack of control of psychopathology in the statistical analyses may have influenced the results.

The present study aims to compare global neuropsychological characteristics of child and adolescent BDoff with a group of offspring of parents with no history of bipolar disorder and to assess the influence of psychopathology on neuropsychological performance.

2. Methods

This research was part of *The Bipolar and Schizophrenia Young Offspring Study* (BASYS), a multi-centre, longitudinal naturalistic study which aims to evaluate clinical, neuropsychological and neurobiological variables of child and adolescent offspring of parents with BD or schizophrenia. The study was conducted in two different Child and Adolescent Psychiatry Departments in Spain: the Hospital Clinic of Barcelona and Hospital Gregorio Marañón of Madrid. Psychiatrists of adult units of both hospitals were requested to identify BP parents of children aged 6 to 17 and to ask them if they agreed to be contacted for this study. Exclusion criteria of BP parents consisted of intellectual disability and significant current medical or neurological conditions. Exclusion criteria of BDoff included intellectual disability, significant head injury or current medical or neurological conditions.

A control parent group was recruited through advertisements in primary health care centres and community locations of the same geographical area. The exclusion criteria of control parents were the same as those for BD parents as well as a personal diagnosis of BP or SZ spectrum disorder or a first degree relative with any of these disorders. Parents motivated to participate because of concerns about their children's school performance, emotional or behavioural problems were also ruled out. Offspring of parents meeting these criteria were included in the community control offspring (CC) group, which were compared with the BDoff. The exclusion criteria were the same as for BDoff. Informed written consent was given by all parents or legal guardians and by subjects over 12. Children under the age of 12 provided assent.

The study was approved by the Ethical Review Board of each participating hospital.

2.1. Procedure

The assessment of the participating family was carried out on the same day. A trained psychiatrist assessed the psychopathology of both affected and non affected parents by using the Spanish version of Structured Interview for DSM-IV (SCID- I) (First et al., 1997). Control parents were also interviewed using the SCID-I to confirm the absence of BD. When one control parent was unable to attend the clinical assessment, the psychiatric history was taken from the attending parent. Psychopathology in children was ascertained by child psychiatrists blind to parental diagnosis by using the Spanish version of The Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime version (K-SADS-PL) (Kaufman et al., 1997; Ulloa et al., 2006) administered separately to parents and children. Socioeconomic status was estimated using the Hollingshead Scale (SES) (Hollingshead and Redlich, 1958). Subjects were asked about lifetime use of cannabis and other drugs.

2.2. Subjects

90 child and adolescent BDoff and 107 CC were included. Table 1 shows age, gender, and socio-economic status in BDoff and CC groups.

Lifetime psychopathology was present in 36.7% of the BDoff group and in 17.8% of the CC group. The most prevalent diagnoses in BDoff were attention deficit hyperactivity disorder (ADHD) (17.6%) and mood disorders (15.6%), followed by anxiety disorders (12.2%), disruptive disorders (3.3%) and other psychiatric disorders (2.2%). In the CC group the most prevalent diagnosis was ADHD (7.5%), followed by anxiety disorders (5.6%), mood disorders (4.7%), other psychiatric disorders (3.7%) and disruptive behaviour disorders (1.9%). Three BDoff and 1 CC

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