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

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ABSTRACT

Background: Schizophrenia (SZ) and bipolar disorder (BD) are considered neurobiological disorders which share some clinical, cognitive and neuroimaging characteristics. Studying child and adolescent offspring of patients diagnosed with bipolar disorder (BDoff) or schizophrenia (SZoff) is regarded as a reliable method for investigating early alterations and vulnerability factors for these disorders. This study compares the neuropsychological characteristics of SZoff, BDoff and a community control offspring group (CC) with the aim of examining shared and differential cognitive characteristics among groups.
Methods: 41 SZoff, 90 BDoff and 107 CC were recruited. They were all assessed with a complete neuropsychological battery which included intelligence quotient, working memory (WM), processing speed, verbal memory and learning, visual memory, executive functions and sustained attention.
Results: SZoff and BDoff showed worse performance in some cognitive areas compared with CC. Some of these difficulties (visual memory) were common to both offspring groups, whereas others, such as verbal learning and WM in SZoff or PSI in BDoff, were group-specific.
Conclusions: The cognitive difficulties in visual memory shown by both the SZoff and BDoff groups might point to a common endophenotype in the two disorders. Difficulties in other cognitive functions would be specific depending on the family diagnosis.

1. Introduction

Schizophrenia (SZ) and bipolar disorder (BD) are considered neurobiological disorders with high heritability, ranging between 80% and 85% (Cannon et al., 1998; McGuffin et al., 2003). The two disorders share clinical symptoms (Tamminga et al., 2013) and cognitive impairment in areas such as memory, attention or executive function.

The contribution of neurodevelopmental processes in both disorders has been previously documented (Bortolato et al., 2015), it being suggested that abnormalities may be present from the prenatal period up to adulthood. Given the high heritability of SZ and BD, studying child and adolescent offspring of patients with schizophrenia (SZoff) or bipolar disorder (BDoff) is considered a reliable method for investigating early alterations and vulnerability factors in the two disorders (DelBello and Geller, 2001; Niemi et al., 2003).

Studies conducted with child and adolescent SZoff have found a similar pattern of difficulties to those observed in their schizophrenic relatives but with less severity. The cognitive functions most commonly reported as affected in child and adolescent SZoff are intelligence, attention, verbal memory, working memory and executive functions (Davalos et al., 2004; de la Serna et al., 2011; Erlenmeyer-Kimling et al., 2000, 1993; Ott et al., 1998; Ozan et al., 2010).

Fewer studies have been conducted in child and adolescent samples of BDoff. Some (de la Serna et al., 2016; Diwadkar et al., 2011; Klimes-Dougan et al., 2006), but not all (McDonough-Ryan et al., 2002), have found difficulties in cognitive areas such as attention, processing speed, executive functions, visual memory or spatial memory.

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Previous studies comparing cognitive functions in children and adolescents at risk for SZ or BD have used different methodologies. These include cohort studies (Seidman et al., 2013), high-risk samples of first-degree relatives (Kremen et al., 1998), and samples including offspring whose parents were diagnosed with major affective disorders, not exclusively BD (Erlenmeyer-Kimling et al., 1993, 2000; Wolf et al., 2002).

Schubert and McNeil (2005) investigated neuropsychological differences between a group of young adult SZoff, a group of affective psychosis offspring (mainly with parents with BD) and a normal-risk offspring group. They found that SZoff had lower scores than the normal-risk offspring group on verbal memory, attention and grammatical reasoning. BDoff differed from normal offspring in attention and grammatical reasoning. In another study, Maziade et al. (2009) compared a group of SZoff and BDoff from densely affected families with a group of healthy controls, the mean age being 17.3 years. The results showed that SZoff and BDoff shared impairment in intelligence, verbal memory, visual memory and executive functions, as compared with controls. However, BDoff showed greater difficulties than SZoff in some executive functions.

Research specifically comparing child and adolescent SZoff and BDoff is scarce. Diwadkar et al. (2011) compared SZoff, BDoff and healthy controls with a mean age between 14.0 and 14.9 years, assessing working memory and sustained attention in the three groups. They found that only the SZoff group showed impairment in working memory compared with the healthy control group, whereas the BDoff group showed significant difficulties in sustained attention processing compared with healthy controls.

As already noted, cognitive studies comparing children and adolescent samples at risk of schizophrenia and bipolar disorder have used different methodologies. To our knowledge, there is only one specific study (Diwadkar et al., 2011) performed in child and adolescent samples, and the authors did not include a complete neuropsychological battery.

The aim of this study was to compare neuropsychological characteristics across three offspring groups (SZoff, BDoff and a group of offspring from parents with no psychiatric disorder) in order to examine shared and differential cognitive features among groups.

2. Methods

This study is part of the Bipolar and Schizophrenia Young Offspring Study (BASYS), a multi-centre, naturalistic study which aims to evaluate clinical, neuropsychological and neuroimaging variables in child and adolescent offspring of patients with schizophrenia or bipolar disorder. The research was conducted in two child and adolescent psychiatry departments in Spain: the Hospital Clinic in Barcelona and the Hospital Gregorio Marañón in Madrid. The study was approved by the Ethical Review Board of each participating hospital.

2.1. Sample

Psychiatrists from the adult units of both hospitals were asked to identify SZ or BD probands with children aged between 6 and 17 years and to ask them if they agreed to be contacted for this study. Exclusion criteria for SZoff and BDoff were intellectual disability, significant head injury or current medical or neurological conditions. The final sample consisted of 90 BDoff and 41 SZoff.

A control parent group was also recruited through advertisements posted in primary health care centres and other community locations within the same geographical area. The exclusion criteria for the community control offspring (CC) were the same as for the high-risk subjects plus a first or second-degree family history of BD or SZ spectrum disorders. The final control sample included 107 CC offspring. Further details about the description of the samples and the recruitment method can be found elsewhere (Sanchez-Gistau et al., 2015).

Lifetime psychopathology was present in 58.5% of SZoff, 36.7% of BDoff and 17.8% of CC participants. The most prevalent diagnoses in SZoff were attention deficit hyperactivity disorder (ADHD) (46.3%), anxiety disorders (17.1%), disruptive disorders (14.6%), mood disorders (4.9%) and other psychiatric disorders (4.9%). In BDoff the most prevalent disorders were ADHD (17.6%), mood disorders (15.6%), anxiety disorders (12.2%), disruptive disorders (3.3%) and other psychiatric disorders (2.2%). In CC the most prevalent diagnoses were ADHD (7.5%), anxiety disorders (5.6%), mood disorders (4.7%), other psychiatric disorders (3.7%) and disruptive disorders (1.9%). A detailed description of the psychopathology in offspring groups and controls can be found in Sanchez-Gistau et al. (2015).

2.2. Clinical assessment

A trained psychiatrist assessed both affected and non-affected parents for psychopathology using the Spanish version of the Structured Clinical Interview for DSM-IV disorders (SCID-I) (First et al., 1997). Control parents were also interviewed using the SCID-I. Children's psychopathology was explored by child psychiatrists blind to the parental diagnosis 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), which was administered separately to parents and children. Socioeconomic status was estimated using the Hollingshead Scale (SES) (Hollingshead and Redlich, 1958).

2.3. Neuropsychological assessment

The cognitive assessment included the following tests:

- Intelligence quotient (IQ) was assessed using the Spanish version of the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) (Wechsler, 2003). This is an intelligence battery designed to evaluate intellectual abilities in children and adolescents aged between 6 and 16 years old. The WISC-IV provides four composite scores: the Verbal Comprehension Index (VCI), the Perceptual Reasoning Index (PRI), the Working Memory Index (WMI) and the Processing Speed Index (PSI). Previous research has shown that the WMI and PSI may be impaired in SZoff (Niemi et al., 2003) and BDoff (Duffy et al., 2009; Gotlib et al., 2005). In order, therefore, to avoid the influence of each of these indexes on the full-scale IQ, the General Ability Index (GAI), derived from the VCI and PRI, was used as an index of intelligence level (Flanagan and Kaufman, 2008).
- Verbal memory was tested with the TOMAL-Memory and learning test (Reynolds and Bigler, 2001): TOMAL is a validated battery designed to assess memory within the age range of 5 to 19 years. Two subtests of this battery were used: Selective Recall of Words and Story Recall.
- Visual memory was assessed by means of the Wechsler Memory Scale R (WMS-R) (Wechsler, 1997): specifically, the Visual Reproduction subtests of the WMS-R were used to provide a measure of immediate and delayed visual memory. Due to the fact that this test is validated in the population over 16 years of age, direct scores were used for statistical analysis. In order to evaluate perceptual organization of complex visual stimuli, the Rey Complex Figure (RCF) (Rey, 1964) was also included in the assessment.
- Attention was assessed with the Conners' Continuous Performance Test (CPT II; Conners, 2000), which is designed to assess sustained attention. Omissions, hit reaction time, variability of standard error, attentiveness and perseverations were included in the statistical analysis.
- Executive functions were evaluated with the Wisconsin Card Sorting Test (WCST), considered to provide a measure of planning strategies, as well as via the interference part of the Stroop test (Golden, 1978), which assesses the ability to inhibit an automatic response (Heaton et al., 1997)

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