



Research report

Pediatric bipolar disorder in a Spanish sample: Features before and at the time of diagnosis

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ABSTRACT

Introduction: Bipolar disorder (BD) often starts in childhood or adolescence. Diagnostic delay is common and may have a negative impact on treatment response and outcome.

Objectives: To describe the clinical characteristics and symptoms of children with BD prior to their diagnosis and at the time of diagnosis in a sample in Spain.

Methods: We retrospectively reviewed the medical records of all children and adolescents ($N = 38$) with a DSM-IV diagnosis of BD evaluated in the Child & Adolescent Psychiatry Unit, University of Navarra, over a 6-year period. We collected the DSM-IV symptoms of BD prior and at the time of diagnosis using the K-SADS-PL interview template.

Results: BD was diagnosed in close to 4% of clinic patients. Thirty (79%) were boys and 8 (21%) were girls; 17 (44.7%) had BD-1, 2 (5.3%) BD-2, and 19 (49.9%) BD-NOS. Median age at diagnosis was 13.9 (10.6; 15.9). Delay of diagnosis was 1.5 (0.7; 3.4) years. Symptoms of BD were similar to those reported in U.S. samples with high rates of severe irritability (94.6%) and psychiatric comorbidity: 92.1% of the BD children had at least one comorbid disorder and 18.4% had three comorbidities, most frequently ADHD (21%) and substance abuse (18.4%).

Conclusions: Clinical findings in this Spanish sample of children with BD closely resembles those described in U.S. clinics. Diagnostic delay, as in the U.S., and frequent misdiagnosis may explain low prevalence estimates found outside the U.S.

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1. Introduction

The prevalence of bipolar disorder (BD) in adults is estimated to be between 1 and 2% (Akiskal, 1995; Kessler et al., 1994). To our knowledge only one community study evaluated the prevalence of BD spectrum in adolescents and found a prevalence rate of about 1% in youth between ages 14

and 18 years (Lewinsohn et al., 1995). However, the prevalence of BD in clinic samples has been estimated to range from 1% to 15% depending on the diagnostic method and instruments used (Geller, 2001a,b; Biederman et al., 1995; Strober et al., 1995).

In a study reviewing the prevalence of BD in children, we found lower prevalence in studies outside the U.S. than those found in U.S. samples (Soutullo et al., 2005). The prevalence of BD in epidemiological community samples outside the U.S. ranged from 0% in the U.K. (where the assessment instrument used had no questions about (hypo)mania (Meltzer et al., 2000), to 1.9% in Holland (Verhulst et al., 1997). The prevalence in outpatient samples ranged from 0% in the U.K. to 7% in Brazil, and in inpatient samples ranged from 0.0006% in Finland, to

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1.2% in Denmark (Thomsen et al., 1992) to 2.5–4.2% in India (Alexander and Raghavan, 1997; Reddy et al., 1997). There is a growing body of evidence about pediatric BD in international samples (Somer Diler, 2007; Holtmann et al., 2008).

However, retrospective studies in the U.S. show that about 60% of adults diagnosed with BD had the onset of bipolar symptoms prior to age 20 years, and up to 20% had the onset of bipolar symptoms prior to age 10 years (Egeland et al., 2002; AACAP, 2007; Lish et al., 1994; Loranger and Levine, 1978). A questionnaire administered in 12 European countries (Finland, Spain, Portugal, Austria, Italy, France, Switzerland, U. K, Hungary, Russia and the Netherlands) found that 33.1% of adult bipolar patients (age 18–83 years) reported an onset of illness prior to age 20 years (Morselli et al., 2003).

Taken together, these findings strongly support the idea that a sizeable number of children may be affected with BD, and suggest that the wide differences in prevalence rates within and outside of the U.S. may be due to underdiagnosis of BD in children.

Other reasons that may explain these prevalence discrepancies across different studies include the use of ICD-10 diagnostic criteria (narrower than those of DSM-IV), ongoing clinician bias against a diagnosis of BD in childhood or adolescence (false negatives or underdiagnosis outside the U.S.), the phenomenological presentation of bipolar disorder in childhood may be different than “classic” euphoric and episodic adult mania could lead to underrecognition (false negative). It could also be due to a true higher prevalence in the U.S. compared to European samples (true positive), or to overdiagnosis in the U.S. (false positives in the U.S.) (Soutullo et al., 2005).

Pediatric bipolar disorder may present differently from the adult form (Biederman et al., 1998; Kowatch et al., 1998). Available studies indicate that mania in children is frequently characterized by severe irritability, ‘affective storms’, or intense and prolonged rages. In addition, the course may be more chronic with complex cycling rather than clearly episodic with inter-episodic euthymia. Children with bipolar disorder may be more likely to present with mixed state, psychotic symptoms and treatment resistance (Wozniak et al., 2005).

Currently there are different working hypothesis, such as the definition by Geller et al. (2002) using elation and grandiosity as cardinal symptoms; the narrow, wide and intermediate phenotypes proposed by Leibenluft et al. (2003); the detailed description of the different types of irritability across diagnoses by Mick et al. (2005); and the use of unmodified DSM-IV criteria that considers either elation or irritability as criterion A symptoms and does not require any of the criterion B symptoms (e.g. grandiosity) by Wozniak et al. (2005) and Biederman et al. (2004). Despite these areas of disagreement, there is considerable evidence available supporting the validity of the bipolar diagnosis in children and adolescents (Youngstrom et al., 2008; Kowach et al., 2005; Axelson et al., 2006). Also, children with bipolar disorder may be misdiagnosed with other comorbid conditions such as ADHD, anxiety disorders, oppositional defiant disorder and conduct disorder. As comorbidity is common in childhood bipolar disorder and symptoms of these disorders often overlap with bipolar disorder, underdiagnosis and misdiagnosis are likely to occur (Tillman et al., 2004; Geller et al., 2002; Biederman et al., 1998; Geller et al., 1998).

There are some studies on the prodromal manifestations of bipolar disorder that may include subtle mood regulation difficulties, symptoms of ADHD, of major depression or of dysthymia (Chang et al., 2000); higher rates of other affective and disruptive behavior disorders as well as subsyndromal psychopathology (Singh et al., 2007), and non-specific psychiatric symptoms (Rucklidge, 2008), such as anxiety, poor attention in school, excitability, hyper-alertness, mood lability, stubbornness, and somatic complaints, problems at school, and also “manic-like” behaviors at the 10-year follow-up: high energy, decreased sleep, problems with thinking/concentration, and excessive and loud talking (Shaw et al., 2005). However, to date, these prodromes are now well defined and are very non-specific.

The main objective of this study was to describe the clinical characteristics and symptoms of children with BD prior to their diagnosis and at the time of first diagnosis in a sample in Spain. We hypothesize that when we apply DSM-IV criteria to children in a clinic setting a sizeable number of children and adolescents will be identified with bipolar disorder. We also hypothesized that the clinical picture of pediatric BD will be characterized by high levels of irritability and psychiatric comorbidity.

2. Method

This research protocol was evaluated and approved by the Department of Psychiatry and the University Hospital, College of Medicine, Institutional Review Board (IRB). We retrospectively reviewed the charts of all children and adolescents with diagnosed BD evaluated in our Unit from 1999 to 2005. These children were selected from an outpatient clinic sample of 774 children and adolescents evaluated (1st evaluation) at the Child & Adolescent Psychiatry Unit, Department of Psychiatry & Medical Psychology at the University Hospital, University of Navarra, Pamplona, Spain. Inclusion criteria were: age <18 years old, a DSM-IV-based diagnosis of BD, and ability to communicate with the medical team. We excluded patients with symptoms of BD due to a medical condition, or due to a substance. A Child & Adolescent Psychiatrist (CAS) and his Fellow (IEC) both retrospectively reviewed the medical records of all patients included in the sample. We collected demographic, Axis I comorbidity, and psychopharmacological treatment data prior to and at the onset of the BD diagnosis. Clinicians used a semistructured interview based on the DSM-IV (APA, 1994) and K-SADS-PL items (Kaufman et al., 1997) to evaluate mood, anxiety, and ADHD-ODD-CD symptoms in children based on chart notes. DSM-IV symptoms were collected prior to and at the time of diagnosis following the K-SADS-PL interview template, Spanish translation (De la Peña et al., 2002; Ulloa et al., 2006). We also computed the diagnostic delay (time from onset of symptoms that met criteria for the diagnosis), the total follow-up time, and the family psychiatric history (collected from the clinical interview).

2.1. Statistical analyses

We used Shapiro–Wilks test to evaluate the normality of the quantitative variables. As most variables had an asymmetric distribution we present them as median and interquartile range (IQR Q25;Q75), and we used non-parametric

Table 1
Sociodemographic and school characteristics of 38 children with BD.

Variable	Median (IQR Q25;Q75) ^a or N (%) ^b
Age of first symptoms (years) ^a	11.57 (8.79;11.66)
Age of first consultation	13.60 (10.33;15.31)
Age of BP diagnosis	13.96 (10.64;15.84)
Sex (girl:boy) ^b	8 (21%):30 (79%)
Ethnic origin ^b	
Caucasian	35 (92.1%)
African	1 (2.6%)
Hispanic	1 (2.6%)
Árabic	1 (2.6%)
Years of education ^a	8 (6;9)
School problems ^b	
0 problems	12 (31.6%)
1 problems	18 (47.4%)
+ 2 problems	8 (21.1%)
Required tutoring	8 (21.1%)
Required academic accommodations (lower expectations)	4 (10.5%)
Repeated a grade	16 (42.1%)
Left school	7 (18.4%)
Residency ^b	
Small to mid-size towns	14 (36.8%)
Urban (city>250,000)	24 (63.2%)

^a Quantitative variables presented as media (inter-quartile range (IQR)): (Q25;Q75).

^b Qualitative variables presented as N (%).

methods on the statistical analysis. We used Wilcoxon exact *p* test to analyse the differences between quantitative variables when the sample was coupled, Mann–Whitney's test for two independent samples, and Kruskal Wallis test for three or more independent samples. Qualitative variables are presented as *N* (%). We used exact *p* tests for non-parametric variables and considered significant a bilateral *p* value <0.05. Data were processed using Windows SPSS-12 (Chicago, Illinois, 2006), and statistical analyses were done by our statistical consultant Marta García-Granero, Ph.D.

3. Results

3.1. Sociodemographic characteristics

We found 38 children and adolescents who met diagnostic criteria for DSM-IV bipolar disorder. This represented 5% of our outpatient clinic sample (*N* = 774). The sociodemographic, ethnic and educational characteristics of our sample are shown in Table 1. The median age (IQR Q25;Q75) at the time of their first clinic evaluation was 13.6 years (10.3;15.3). Thirty (79%) bipolar children were male, 35 (92.1%) were Caucasian, and 63.2% lived in a city (>250,000 inhabitants). The median (IQR Q25;Q75) grade that the patients were attending was 8th grade (6;9). However, only 31.6% of children had no school problems, 42.1% had repeated a school year, and 18.4% had already left school (Table 1).

Seventeen (44.7%) children had a diagnosis of bipolar type I disorder (BP-1), two (5.4%) had BP-2, 19 children (49.9%) had BP-NOS, mostly due to lack of duration of episodes with full symptoms, six (15.8%) of these patients had BP-3 (bipolar disorder secondary to SSRI antidepressant use that did not improve upon stopping the SSRI), and one (2.5%) patient had BP-4 (recurrent irritable depression, with some symptoms of mania and first degree family history of BP-1) as defined by Akiskal et al. (Akiskal, 2007; Akiskal and Pinto, 1999).

3.2. Age of onset and diagnostic delay

Seventy five percent of patients manifested their first symptoms of BD before they were 12 years (median 11.6 (8.79;11.7)), 50% of them were evaluated before they were 14 (10.33;15.31) years old. Thus, 50% of the sample had a diagnostic delay of at least 1.5 years (0.65;3.41) from onset of their first symptoms of BD to the diagnosis, but 25% of the children waited 3.4 years from onset of symptoms to get a diagnosis, mostly due to a delay in getting to see a psychiatrist.

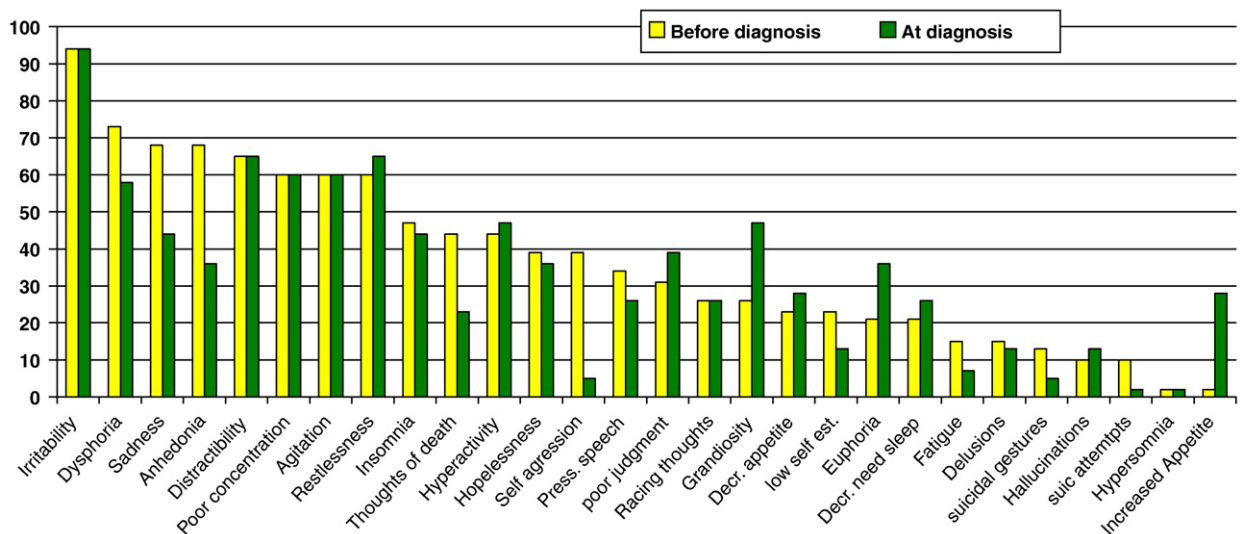


Fig. 1. Prevalence (%) of mood (mania and depression) symptoms before and at the time of BP diagnosis in 38 children.

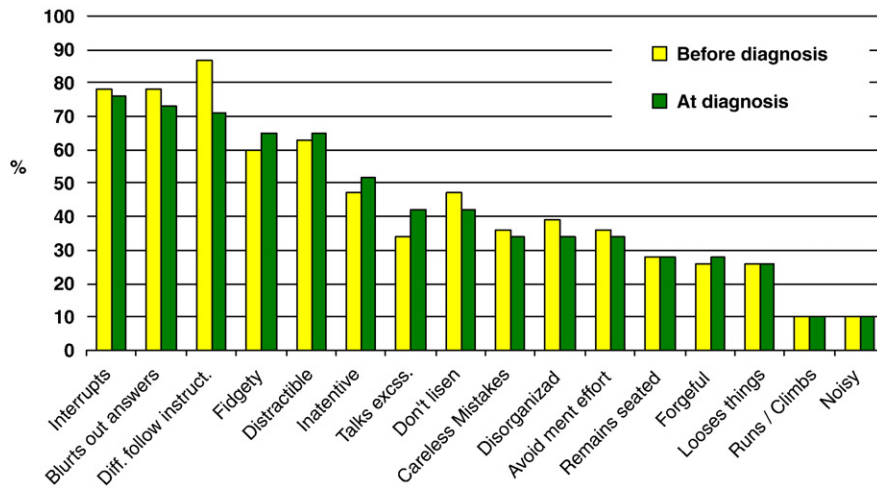


Fig. 2. Prevalence (%) of ADHD symptoms before and at the time of BP diagnosis in 38 children.

3.3. Family psychiatric history

76.3% of patients had at least one first degree relative with a psychiatric disorder, 39.5% had a family history of a mood disorder in a parent and 50% of the children had a history of a psychiatric disorder in a second degree relative.

3.4. Symptoms before diagnosis and at the time of diagnosis of mania

The most common mood symptoms before the diagnosis of BD were: irritability (severe) (94.7%), dysphoria (73.7%), depressed mood (68.4%), anhedonia (68.4%), distractibility (65.8%), poor concentration (60.5%) and psychomotor agitation (60.5%) (Fig. 1). The most common symptoms of mania and depression at the time of diagnosis of BD were: severe

irritability (94.7%), distractibility (65.8%), psychomotor agitation (60.5%), poor concentration (60.5%), and dysphoria (57.9%) (Fig. 2). Only depressed mood and anhedonia were significantly more frequent before the diagnosis ($p < 0.05$) compared with their frequency at the time of the diagnosis. Although grandiosity was more frequent at the time of diagnosis than before the diagnosis, this difference was not statistically significant ($p = 0.057$) (Fig. 1).

The more frequent ADHD symptoms before diagnosis in the BD patients were: difficulty following instructions (86.8%), blurts out answers (78.9%), distractibility (65.8%), fidgetiness (60.5%), and difficulty waiting turns (55.3%) (Fig. 2).

The more frequent ADHD symptoms at the time of diagnosis were: blurts out answers (73.7%), difficulty following instructions (71.1%), distractibility (65.8%), fidgetiness (65.1%), inat-

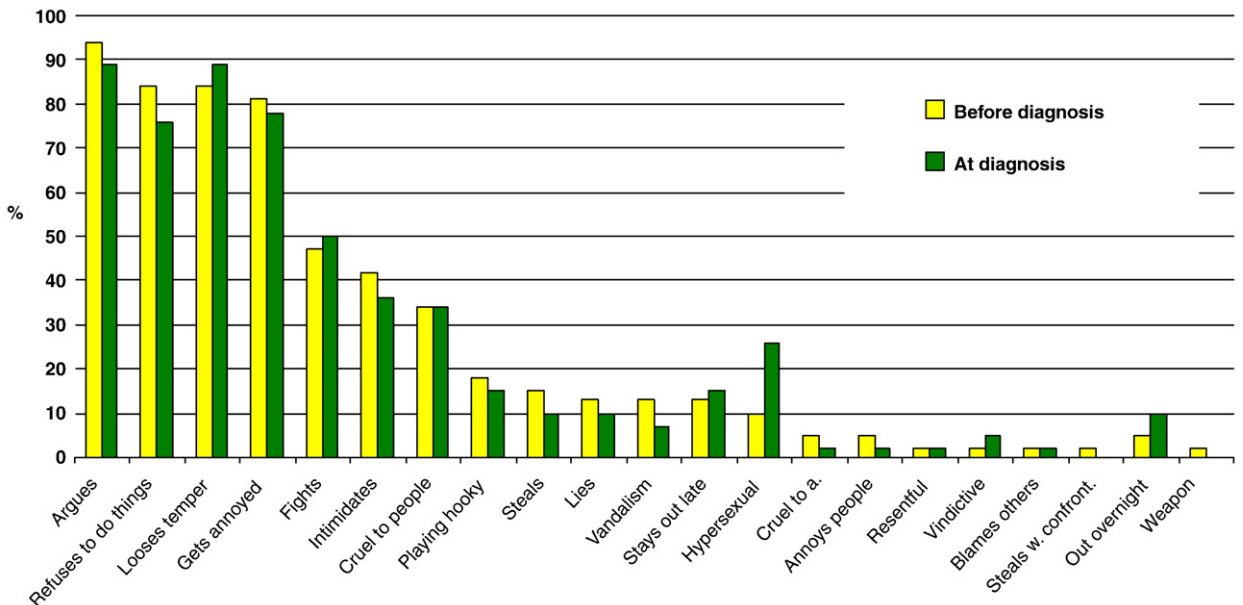


Fig. 3. Prevalence (%) of CD/ODD symptoms before and at the time of BP diagnosis in 38 children.

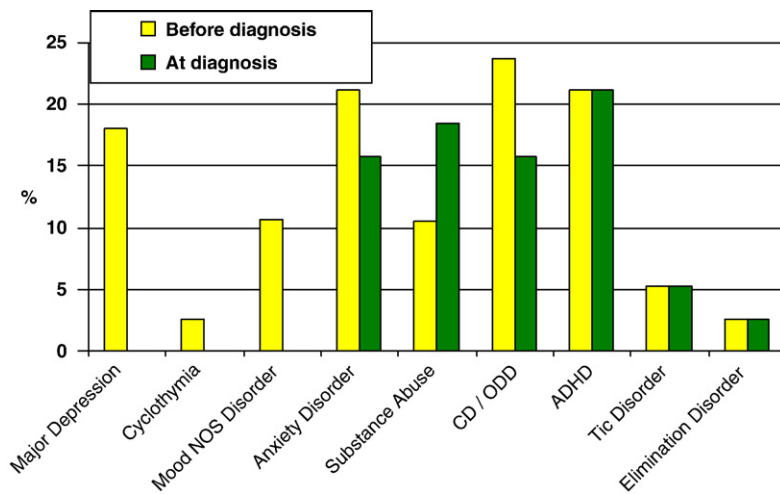


Fig. 4. Diagnoses received before and at the time of bipolar disorder diagnosis in 38 children.

tentive (52.6%) and talks excessively (42.1%) (Fig. 2). We found no significant differences in the frequency of presentation of ADHD symptoms before and at the time of diagnosis.

The most frequent symptoms of ODD or CD before diagnosis were: argues with adults (94.7%), loses temper (84.2%), refuses to do things (84.2%), and gets easily annoyed (81.6%) (Fig. 3). The most frequent symptoms at the time of diagnosis were very similar, and we found no significant differences before and after the diagnosis.

3.5. Comorbidity and previous psychiatric disorders

76.2% of the children in our sample had been previously diagnosed with at least one psychiatric disorder before receiving the diagnosis of BD: 12 (31.6%) with one, 12 (31.6%) with two, 4 (10.5%) with four and 1 (2.5%) with five

different disorders. At the time of diagnosis, 92.1% of children had at least one comorbid psychiatric disorder: 1 (2.6%) had five different comorbid psychiatric disorders in addition to BD, 6 (15.8%) had three, 10 (26.3%) had two disorders and 18 (47.4%) had only one comorbid psychiatric disorder.

The most frequent psychiatric disorders present before the diagnosis of BD were: ADHD (21.1%), major depression (18.4%) and ODD (15.8%), followed by CD (10.5%), substance use disorder, separation anxiety and mood disorder NOS, all present in 4 (10.5%) patients, and cyclothymia (2.6%) (Fig. 4). The most frequent psychiatric disorders present at the time of diagnosis were: ADHD (21.1%) and substance abuse disorder (18.4%) followed by disruptive behavior disorders (CD/ODD) and anxiety disorder that were present in 15.8% patients (Fig. 4).

We only found significantly different the frequency of major depression before (16.5%) versus at the time of

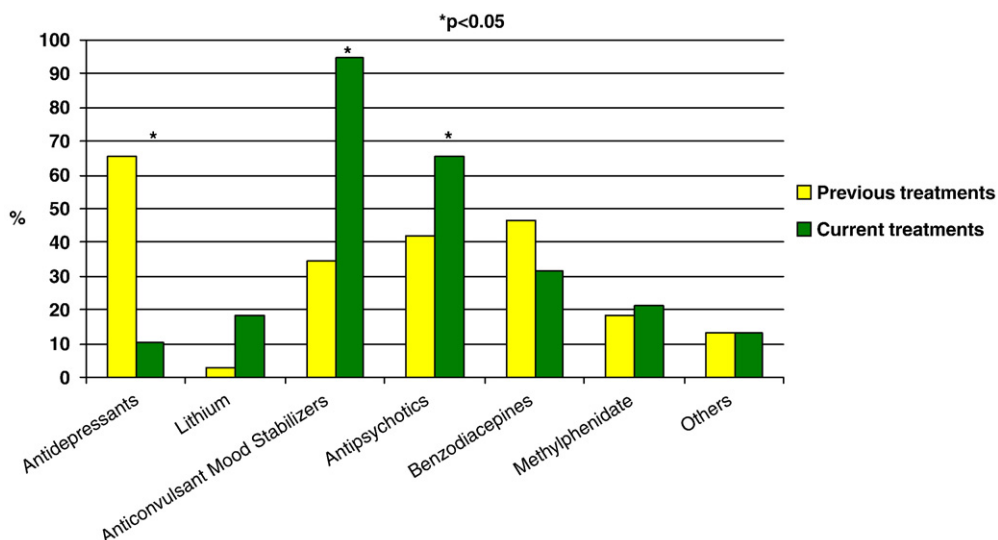


Fig. 5. Treatment received before and at the time of bipolar disorder diagnosis in 38 children.

diagnosis (0%) of BD ($p = 0.016$). The frequency of any anxiety disorders was higher, but not significant, before the diagnosis of BD (Fig. 4).

3.6. Treatment received before and at the time of diagnosis

92.1% of all children diagnosed with BD had received some pharmacological treatment before the diagnosis of BP: 1 (2.6%) had received up to five different psychopharmacological treatments, 5 (13.2%) four, 12 (31.6%) three, 7 (18.4%) two and 10 (26.3%) only one treatment. At the time of diagnosis all patients had received pharmacological treatment: 2 (5.3%) had received up to five types of different treatments, 5 (13.2%) had received four, 10 (26.3%) had received three, 16 (42.1%) have received two, and 5 (13.2%) had received only one.

The most frequent agents received before BD diagnosis were antidepressants: 65.8% of children had received antidepressant treatment before diagnosis versus only 4 (10.5%) at the time of diagnosis ($p < 0.05$) (Fig. 5). The most frequent treatments received at the time of diagnosis were: anticonvulsant mood stabilizers 36 (95.7%), and antipsychotics: 25 (65.8%), versus, only 13 (34.2%) and 16 (42.1%) respectively before the diagnosis ($p < 0.05$) (Fig. 5). 47.4% of children had received benzodiazepines before diagnosis (47.4%) versus only 21.1% at the time of diagnosis, but this difference was not significant ($p > 0.05$).

4. Discussion

Consistent with samples from the U.S. and elsewhere this study of clinic referred youth in Spain found that severe irritability was the most frequent mood symptom at the time of diagnosis (in 94.6% of patients), similar to the frequency found in a recent meta-analysis (Kowach et al., 2005). Only 36% of our patients had euphoria at the time of diagnosis, and 47% had grandiosity. The frequency of euphoria (70%) and grandiosity (78%) in Kowach's study is higher than in our sample (36% and 47% respective). The reason for these discrepant findings may be methodological differences across studies. While our study used unmodified DSM-IV criteria, some studies in Kowach's et al. (2005) meta-analysis used Geller's (2001b) WASH-U-K-SADS criteria, that require at least one symptom of euphoria or grandiosity, and thus will find higher rates of these symptoms. In fact, studies that use unmodified DSM-IV criteria (Wozniak et al., 1995) reported much lower rates of euphoria (14%) than those reported by Geller et al. (2002) (70%). Some researchers favour the need to require at least one *cardinal symptom* (usually grandiosity or euphoria) for a pediatric BP diagnosis to potentially increase the specificity and reduce false positives (Geller et al., 2002). However this approach may decrease sensitivity and increase false negatives. 94% of the children in our study had irritability, 47.4% had grandiosity (all of them also had irritability), and 36.8% had euphoria (23.6% had euphoria + grandiosity + irritability, and only 13.2% had euphoria without irritability). Consequently, if we had required the presence of euphoria or grandiosity, only 60.6% of our patients would have been diagnosed as BD, and 39.4% probably would have been diagnosed with ODD/CD or MDD. This decision has important therapeutic and prognostic implications, and failing to differentiate unipolar MDD from bipolar disorder can have serious consequences for the child and his family.

Thus, to increase the specificity in the diagnosis of pediatric BP it may be more important to assess the quality of the irritability, rather than to focus on putative *cardinal symptoms*. Mick et al. (2005) described that episodic severe/extreme/explosive/violent irritability is more frequent in children with BD. A less severe irritability was more frequently associated with ODD and depression. Patients in our study presented extreme explosive unprovoked irritability.

Hypersexuality, without history of sexual abuse, may be fairly specific for BD, but the absence of this symptom does not rule out the diagnosis. Only 23% of children in our sample had hypersexuality at the time of diagnosis, slightly lower than the 38% in Kowach's et al. (2005) meta-analysis.

Psychotic symptoms also may lead to misdiagnosis in pediatric BD. 13.2% of children in our sample had psychotic symptoms (delusions or hallucinations). The frequency of psychotic symptoms in BD children in the literature ranges widely from 16% to 60% (Kowach et al., 2005; Geller et al., 1998; Wozniak et al., 1995). This variability may be due to methodological differences or to clinical differences between samples, such as a higher prevalence in inpatients (Kowach et al., 2005; Pavuluri et al., 2005). Some authors found a higher prevalence of psychotic symptoms in children and adolescents than in adults (McElroy et al., 1997), but other studies found higher prevalence of psychosis in adults (Geller et al., 2002; Goodwin and Jamison, 1990). This discrepancy may be the result of children and adolescents with psychotic symptoms being erroneously diagnosed with schizophrenia and other psychotic disorders (Joyce, 1984). Major depression (11.8%) and bipolar disorder (10.9%) were more frequent than schizophrenia (10%) in children and adolescents with a first psychotic episode in Spain (Castro-Fornieles et al., 2007).

In our sample, the most frequent mood symptoms before the diagnosis of BD were: irritability (94%), depressed mood (68%), and anhedonia (68%). The only symptoms that decreased significantly at the time of diagnosis were the depressive symptoms: depressed mood (68.4% versus 42.7) ($p = 0.013$) and anhedonia (68.4% versus 42.7) ($p = 0.002$). The high frequency of depressive symptoms may explain the diagnostic delay.

Concerning the polarity of the first episode, some studies show that the first episode is more frequently depressive in younger subjects (63.6% in subjects younger than 13) (Soutullo et al., 2002). However, other researchers found that only 30% of bipolar children presented first with a depressive episode (Biederman et al., 2004), although an additional 30% of bipolar children presented first with a mixed episode. In our sample 18% of children had been previously diagnosed with major depression and 30% of them with other mood disorders (cyclothymia or mood disorder not otherwise specified). It is possible, given the high rate of manic symptoms present prior to BD diagnosis that some of these children had a mixed episode but were diagnosed instead as unipolar MDD.

Our data suggest that the most frequent mood alteration before bipolar diagnosis includes depressive or mixed characteristics. The presence of depression may be a risk factor for the diagnostic delay, and may lead to SSRI treatment.

Our study found that at least 50% of children had a 1.5 year diagnostic delay, and 25% had a 3.5 year diagnostic delay, however this delay is much lower than the 10 years found by

Egeland et al. (2002) and Lish et al. (1994). The diagnostic delay may be explained by several factors. First, the acceptance of pediatric BD in the U.S. is growing over the last 15 years, but some studies suggest that this acceptance may still be lacking in some parts of Europe (Soutullo et al., 2005; Pavuluri et al., 2005). In our study a reluctance to diagnose BD in children can be a factor, considering that 21% of the children had euphoria and 26% had grandiosity prior to the diagnosis, and even these children were not diagnosed as BD. In our sample the age of first consultation (almost 14 years) was slightly older than that reported in other studies.

Second, the presence of some initial symptoms of BD may be considered a “normal part of adolescence”. In our sample half of the children were older than 14, thus it is possible that their parents looked for academic and family stressors to explain the symptoms, and they delayed psychiatric evaluation.

Thirdly, some children could have been misdiagnosed with other disorders. We found high levels of comorbidity, similar to other studies (Soutullo et al., 2002; Kowach et al., 2005). The frequency of ADHD comorbidity in our sample was 21%, slightly lower to the range in Kowach's meta-analysis (29–87%), but much lower than the mean (62%). This difference could be explained by the fact that more than half of our patients were adolescents, and ADHD is highly comorbid in childhood-onset BD (90%), but less common (57%) in adolescent-onset BD (Findling et al., 2001; McClellan et al., 1999; Faraone et al., 1997; Wozniak et al., 1995; Lewinsohn et al., 1995). Substance abuse disorder (SUD) was one of the most frequent comorbid disorders in our sample (18.4%) at the time of diagnosis, other studies found comorbidity with SUD in 0% to 40% of youth with BD (Pavuluri et al., 2005). Wilens et al. (2004) found that the risk of SUD is up to 8 times higher in adolescent-onset BD compared with childhood-onset BD, thus the adolescent age of our sample may explain the high prevalence of comorbid SUD.

The frequency of comorbid disorders in the literature ranges from 12.5%–56% for anxiety disorders, to 46.2%–75% for ODD, and 5.6%–37% for CD (Pavuluri et al., 2005). Some authors found a higher prevalence of comorbid anxiety disorders in adolescents than in children (Birmaher et al., 2002; Biederman et al., 1997). In our study the prevalence of ODD was only 15%, at the low end of reported ranges. Similar to other samples (Pavuluri et al., 2005), the comorbidity with eating, tic, or elimination disorders was very low in our sample.

5. Limitations

This study has some important methodological limitations. Most importantly most data were collected retrospectively in chart reviews. Children received clinical evaluations using DSM-IV criteria and a semistructured DSM-IV-based clinical interview to screen for ADHD, mood and anxiety disorders. We then used the K-SADS-PL template to search for the symptoms present at the time of diagnosis and prior to the diagnosis of bipolar disorder (Kaufman et al., 1997; De la Peña et al., 2002; Ulloa et al., 2006). Also, our sample size can be considered low compared to the North-American samples, however, compared to non-U.S. samples this sample size can be considered representative of an outpatient clinic.

6. Conclusions

Findings in this sample of BD children in an outpatient clinic in Spain closely resemble those described in U.S. samples, with high levels of severe irritability, mixed states and comorbidity, that have been called an atypical presentation. Fifty percent of children presented a delay in diagnosis of at least 1.5 years, and 25% more than 3.5 years, even though mood symptoms were present. The diagnostic delay may be due to this atypical presentation (irritability and mixed episodes) or to the complex comorbidity. The mood alteration before bipolar diagnosis was often mixed: 94% had severe irritability, and 68% sadness or anhedonia. Bipolar illness in children in our sample was highly comorbid: 92.1% of children with BD had at least one comorbidity, and 18.4% had at least three. Children with BD had received treatment with many different medications before the diagnosis of BD. The high rate of diagnosis and symptoms of depression in our sample, and the frequent use of antidepressants prior to BD diagnosis suggest that the differential diagnosis of unipolar depression and mixed episode bipolar disorder may be a difficult clinical challenge. Furthermore, the high rates of comorbidity, both before and at the time of BD diagnosis may complicate the clinical picture and make it difficult for clinicians to diagnose BD. It is difficult to say if the symptoms or psychiatric comorbidity found retrospectively prior to the diagnosis of BD represent prodromes of the disorder, or are the disorder itself that is not yet recognized. Our study suggests that clinical characteristics and comorbidity, which have been implicated in underdiagnosis in the U.S., may also explain the low estimates of prevalence of pediatric BD outside of the U.S.

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Conflict of interest

Cesar Soutullo, M.D., Ph.D. (1996–2008)

Dr. Cesar Soutullo has received research funding from: Abbott, Alicia Koplowitz Foundation, Bristol-Myers Squibb, Eli Lilly, Gobierno de Navarra, Carlos III Institute (FIS): Redes Temáticas de Investigación Cooperativa, Pfizer, PIUNA, Stanley Medical Research Institute-NAMI, and Solvay.

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He has served on the speaker's bureaus of: Asociación Navarra ADHI, ACANPADAH, APNADAH, AstraZeneca, ASTTA, CC.AA.: Asturias, Castilla y León, Madrid; Eli Lilly, Fundación Innovación Social de la Cultura, GlaxoSmithKline, Grupo Aula Médica, Janssen-Cilag, Novartis, SEP-SEPB, Sociedad Vasco-Navarra Psiquiatría, and Solvay.

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Immaculada Escamilla-Canales, M.D., Ph.D.

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Janet Wozniak, M.D. (2006–2008)

Dr. Janet Wozniak is the author of “Is Your Child Bipolar?”, published May 2008, Bantam Books.

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*Joseph Biederman, MD, Narrative Disclosure Statement
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Dr. Joseph Biederman is currently a consultant/advisory board member for the following pharmaceutical companies: Janssen, McNeil, Novartis, and Shire.

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