

Journal of Attention Disorders

<http://jad.sagepub.com/>

Bipolar Disorder in Children With ADHD: A Clinical Sample Study

Renato Donfrancesco, Michela Di Trani, Elda Andriola, Daniela Leone, Maria G. Torrioli, Francesca Passarelli and Melissa P. DelBello

Journal of Attention Disorders published online 11 July 2014

DOI: 10.1177/1087054714539999

The online version of this article can be found at:

<http://jad.sagepub.com/content/early/2014/07/08/1087054714539999>

Published by:



<http://www.sagepublications.com>

Additional services and information for *Journal of Attention Disorders* can be found at:

Email Alerts: <http://jad.sagepub.com/cgi/alerts>

Subscriptions: <http://jad.sagepub.com/subscriptions>

Reprints: <http://www.sagepub.com/journalsReprints.nav>

Permissions: <http://www.sagepub.com/journalsPermissions.nav>

Citations: <http://jad.sagepub.com/content/early/2014/07/08/1087054714539999.refs.html>

>> [OnlineFirst Version of Record](#) - Jul 11, 2014

[What is This?](#)

Bipolar Disorder in Children With ADHD: A Clinical Sample Study

Journal of Attention Disorders
1–6
© 2014 SAGE Publications
Reprints and permissions:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/1087054714539999
jad.sagepub.com


Renato Donfrancesco¹, Michela Di Trani², Elda Andriola³, Daniela Leone⁴,
Maria G. Torrioli⁴, Francesca Passarelli², and Melissa P. DelBello⁵

Abstract

Objective: To explore the impact of early-onset bipolar disorder (pediatric bipolar disorder [PBD]) on ADHD. **Method:** We compared ADHD symptom severity, ADHD subtype distribution, and rates of comorbid and familial psychiatric disorders between 49 ADHD children with comorbid PBD and 320 ADHD children without PBD. **Results:** Children with ADHD and PBD showed higher scores in the Hyperactive and Inattentive subscales of the ADHD Rating Scale, than children with ADHD alone. The frequency of combined subtype was significantly higher in ADHD children with PBD, than in those with ADHD alone. ADHD children with PBD showed a higher rate of familial psychiatric disorders than ADHD children without PBD. The rate of conduct disorder was significantly greater in children with PBD and ADHD compared with children with ADHD alone. **Conclusion:** ADHD along with PBD presents with several characteristics that distinguish it from ADHD alone, suggesting that these may be distinct disorders. (*J. of Att. Dis.* XXXX; XX(X) XX-XX)

Keywords

prevalence, bipolar disorder, ADHD, children

Introduction

Pediatric bipolar disorder (PBD) may present differently than bipolar disorder (BD) in adults (Geller & DelBello, 2005; Luby & Belden, 2006; Wolf & Wagner, 2003). Particularly, a marker of juvenile PBD is the high rate of comorbidity with ADHD (Barkley & Murphy, 2006; Biederman et al., 1996; Donfrancesco et al., 2011; Faraone & Biederman, 1997; Galanter & Leibenluft, 2008; Kim & Miklowitz, 2002; Sachs, Baldassano, Truman, & Guille, 2000). This comorbidity often leads to severe impairment, with increased impulsivity, psychotic symptoms, need for hospitalization, and school failure (Wolf & Wagner, 2003). The relationship between PBD and ADHD has received considerable attention in psychiatric research. Elevated rates of PBD–ADHD comorbidity among youth and co-aggregation within families raise the question of whether co-occurring PBD and ADHD represent a more severe subtype of either PBD or ADHD or a unique disorder (Miller, Chang, & Ketter, 2013; Singh, DelBello, Kowatch, & Strakowski, 2006). Rates of PBD in children with ADHD vary widely depending on the sample and which assessment approach is used (Pataki & Carlson, 2013). Specifically, a number of reviewers have pointed out that differences in methodologies influence rates of PBD in ADHD samples and rates of ADHD in PBD samples (Carlson, 2011; Galanter & Leibenluft, 2008; Hassan, Agha, Langley, & Thapar, 2011; Pataki & Carlson, 2013). Serrano, Ezpeleta,

and Castro-Fornieles (2013) found that 8% of an ADHD sample met criteria for PBD and 6% for BD—not otherwise specified (BD-NOS).

In the same way, ADHD has been recognized as a prevalent comorbidity in juvenile BD (Sachs et al., 2000; Tamam, Karaku, & Ozpoyraz, 2008). Systematic studies of children and adolescents with a diagnosis of BD show that rates of ADHD range from 57% to 98% (Geller et al., 1995; Kowatch et al., 2005; Tramontina, Schmitz, Polanczyk, & Rohde, 2003), while other study found a prevalence of ADHD of 21.1% in children with BD (Soutullo et al., 2009). These data focus on a bidirectional overlap, even if the percentage of PBD in ADHD children is much lower than the percentage of ADHD in children with BD.

While the rate of ADHD comorbidity in PBD youth appears to be a function of age (Wozniak, 2005), the impact on age of comorbid PBD in ADHD samples is less clear. According to a review article by Wilens et al. (2002),

¹S. Pertini Hospital, Rome, Italy

²Sapienza University, Rome, Italy

³LUMSA University, Rome, Italy

⁴Sacro Cuore University, Rome, Italy

⁵University of Cincinnati, OH, USA

Corresponding Author:

Michela Di Trani, Department of Dynamic and Clinical Psychology,
Sapienza University, Via dei Marsi 78, 00185, Rome, Italy.
Email: micheladitrani@hotmail.com

children with ADHD are 10 times more likely to develop PBD than age-matched and gender-matched controls. However, ethnic and sociocultural differences are meaningful in the emergence of early-onset PBD (Kennedy, Boydell, van Os, & Murray, 2004).

The overlap of diagnostic criteria between PBD and ADHD (e.g., hyperactivity, impulsivity/aggressiveness, distractibility, irritability, and emotional lability) makes the differential diagnosis difficult (Biederman et al., 1996; Milberger, Biederman, Faraone, Murphy, & Tsuang, 1995; Wozniak, 2005).

The relationship between ADHD and PBD is far from clear; three models have been suggested to explain this overlap: (a) ADHD symptoms can be a prodrome to PBD in some patients, (b) PBD and ADHD are distinct disorders but share an association with emotional dysregulation in children, and (c) PBD may be a severe variant of personality traits in which an underlying dysfunction in affective and cognitive circuitry associated with emotion regulation causes both temperamental difficulties and clinical symptoms (West, Schenkel, & Pavuluri, 2008).

Other studies suggest that PBD with ADHD can be a distinct genetic subtype from PBD or ADHD alone (Biederman et al., 2008; Wozniak, 2005). This issue is not merely nosological as ADHD comorbidity affects several clinical features of PBD and it can be a meaningful predictor of prognosis and treatment (Biederman et al., 1996; Faraone & Biederman, 1997; Masi et al., 2004).

In previous studies, some authors explored the effects of ADHD co-occurrence on PBD phenomenology and treatment by analyzing a sample of children and adolescents with PBD, and stratifying them according to the ADHD comorbidity, that is, presence or absence. According to these findings, ADHD was associated with an earlier onset of PBD (Masi et al., 2007), a chronic course and an irritable mood (Masi et al., 2006), a greater resistance to treatments (Masi et al., 2004), a more frequent diagnosis of BD-NOS (Masi et al., 2007), and a lower rate of lithium response (Masi et al., 2010). In another research study of ADHD (Donfrancesco et al., 2011) in children with PBD spectrum, we found that ADHD children with PBD spectrum, compared with those with ADHD alone, showed a higher rate of combined subtype, higher scores of ADHD Rating Scale, and higher rates of major depression, oppositional defiant disorder (ODD), and conduct disorder (CD).

With these considerations in mind, the main aim of the present study is to expand upon these findings in a larger sample of children with ADHD and PBD rather than those with all bipolar spectrum disorders (e.g., BD-NOS). We hypothesized that youth with ADHD-PBD co-occurrence is associated with (a) a greater severity of ADHD symptoms, (b) a greater rate of combined ADHD subtype, (c) a greater frequency of familial psychiatric disorders, and (d) a higher frequency of other comorbidities than those with ADHD alone.

Method

We studied 369 consecutive drug-naïve Caucasian outpatients with ADHD (324 boys and 45 girls, mean age of 8.8 years, $SD = 2.5$), diagnosed at the Clinic for Developmental Neurology and Psychiatry of "S. Pertini Hospital" in Rome, from 2010 to 2013. All participants were in the middle socioeconomic status (SES) level (Hollingshead, 1975), with a mean score of 74.8 ($SD = 13.7$). Parents of participants signed a statement of informed written consent and the privacy policy. In our sample of 369 children with a diagnosis of ADHD, 49 had comorbid PBD (13.28% of the total sample; 46 boys; $M_{age} = 8.54$, $SD = 2.46$; duration of the PBD symptoms: $M = 18.86$ months, $SD = 9.44$) and 320 did not have comorbid PBD (86.72% of the total sample; 278 boys; $M_{age} = 8.80$; $SD = 2.52$). The diagnosis of PBD was defined according to *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev; *DSM-IV-TR*; American Psychiatric Association [APA], 2000) criteria for BD I or BD II, including duration and functional impairment. Bipolar NOS children are excluded. In the group of 49 bipolar participants, 42 were PBD-type 1 and 7 were PBD-type 2. All the children in the ADHD-PBD group showed in the assessment session both ADHD symptoms and mood disorder symptoms. However, the retrospective evaluation confirmed a starting point of bipolar symptomatology, after the onset of ADHD.

Disruptive mood dysregulation disorder (DMDD), according to *DSM* (5th ed.; *DSM-V*; APA, 2013) criteria was not assessed, but the diagnosis of BD was performed following the *DMS-IV-R* criteria.

Regarding the features of BD in our group of children with PBD, the elated mood was more frequent (79.60%) than irritability (65.31%). These data diverge from the data of Wozniak et al. (2005) who found irritability as a cardinal symptom of PBD with a percentage (94%) higher than elated mood (51%). This difference can be explained by cultural features, according to the previous transcultural study (Donfrancesco et al., 2014) about a comparison of PBD in Italy and the United States. Regarding other symptoms of our PBD sample, 61.22% presented grandiosity, 20.41% reported decreased need for sleep, 85.71% were more talkative than usual, 77.55% exhibited racing thoughts, 57.14% showed poor judgment, 65.31% demonstrated increase in goal-directed activity, and none presented psychotic symptoms.

Both children and parents of the samples (ADHD with PBD; ADHD without PBD) participated in three clinical sessions to reconstruct lifetime and medical history and to assess familial psychiatric disorders (only first and second degree siblings are included). They also received a Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997) conducted by an experienced child

psychiatrist (RD). Lifetime comorbid psychiatric disorders were also identified using the K-SADS.

The parents of all participants were also asked to fill out the ADHD Rating Scale Parent Version (ADHD-RS PV) adapted for the Italian population (Marzocchi & Cornoldi, 2000), to explore the severity of ADHD symptomatology. The Wechsler Intelligence Scale for Children–III (WISC–III), Italian version (Orsini & Picone, 2006), was used to estimate the IQ.

Statistical Analysis

Demographic characteristics of children with comorbid ADHD and PBD versus those with ADHD alone were compared using χ^2 analysis for categorical variables and one-way ANOVAs for continuous variables.

One-way ANOVAs were also performed on IQ scores (Total, Performance, and Verbal IQ) and on ADHD Rating Scale scores (Total, Hyperactivity, and Inattention Scales), whereas χ^2 analyses were computed in relation to the distribution of ADHD subtypes, other comorbid diagnoses, including, anxiety disorder, ODD, and CD.

Logistic regressions were used to verify the role of demographic variables, ADHD severity, ADHD subtypes, and the presence of other psychiatric comorbidities on the presence/absence of PBD as a *dummy* variable (respectively codified with 0/1). Specifically, three models were run: The first included, as independent variables, age, sex, IQ, SES, and ADHD Rating Scale PV scores (Total, Hyperactive, and Inattentive scores); the second model included age, sex, IQ, SES, and ADHD subtypes (combined, hyperactive, and inattentive subtypes); the third model included age, sex, IQ, SES, and comorbid lifetime diagnoses (depressive disorders, anxiety disorders, ODD, CD).

Results

No differences in the distribution of sex, age, and SES were found between the ADHD with PBD versus ADHD-alone groups (see Table 1). The first group was composed of 46 boys (93.88%), whereas the second group was composed of 278 boys (86.88%). Mean age of the ADHD group with PBD was 8.54 ($SD = 2.46$), and mean of ADHD group without PBD was 8.80 ($SD = 2.52$).

Moreover, as shown in Table 1, ADHD children with PBD showed higher scores on the Total scale ($F = 9.64$; $p = .00$; effect size = 0.03), Hyperactivity ($F = 20.81$; $p = .00$; effect size = 0.05), and Inattention ($F = 4.25$; $p = .04$; effect size = 0.01) subscales of ADHD Rating Scale than ADHD children without PBD.

Regarding ADHD subtypes distribution, the percentage of combined subtype was significantly higher and the percentage of inattentive subtype was significantly lower in ADHD children with comorbid PBD, compared with children without PBD.

Youth with ADHD and PBD showed higher percentage of lifetime ODD and CD, compared with those with ADHD and without PBD group. Finally, no differences were found in IQ scores between the two groups.

Of the 320 ADHD children without PBD (6.88%), 22 had at least one parent with psychopathology compared with 24 of the 49 ADHD children with PBD (48.98%).

Logistic regressions showed that only high ADHD-RS Hyperactivity score (Cox and Snell Index = .06; $B = 0.17$; $p < .01$) was significantly associated with the presence of PBD in ADHD children, and that only combined subtype was a significant predictor of the presence of PBD (Cox and Snell Index = .02; $B = .76$; $p < .05$). Regarding psychiatric comorbidity, lifetime diagnoses of ODD (Cox and Snell Index = .09; $B = 1.31$; $p < .01$) or CD ($B = 1.03$; $p < .05$) were significantly associated with PBD in ADHD children.

Discussion

The literature strongly suggests that ADHD is associated with very early-onset BD (PBD; Galanter & Leibenluft, 2008; Kim & Miklowitz, 2002). PBD is a crucial issue in current research, as epidemiological studies examining age at onset of the first episode of bipolar illness show that the median age is lower by 4.5 years in participants born in the past 50 years, and that participants with prepubertal onset are significantly higher in the more recent cohorts (Chengappa et al., 2003).

The main aim of the study was to assess the impact of PBD comorbidity in ADHD children. Previous studies reported an overall prevalence of PBD in 0.5% to 30% of ADHD children (Hassan et al., 2011; Tillman & Geller, 2006), but several reviewers have pointed out that differences in methodology influence findings in these rates (Carlson, 2011; Galanter & Leibenluft, 2008; Hassan et al., 2011; Pataki & Carlson, 2013).

In our sample of 369 children, 49 (13.28%) of the participants displayed comorbid PBD. The prevalence of PBD in our sample appears consistent with the literature: Molina et al. (2009) showed rates of 11% to 23% of PBD using lifetime prevalence and the Kiddie-SADS, and Serrano et al. (2013) found an association of 8% for PBD-*DSM* and of 6% for PBD-NOS, resulting in a total comorbidity with PBD of 14%. In a sample of 7- to 13-year-old Turkish children diagnosed with ADHD, Diler, Uguz, Seydaoglu, Erol, and Avci (2007) found that 8.2% had comorbid BD.

According to Donfrancesco et al. (2011), the most prevalent subtype of PBD in ADHD children was the non-cycling disorder.

To clarify the relationship between ADHD and PBD, the two groups were also compared with the following variables: symptoms severity, distribution of ADHD subtypes, other comorbid diagnoses, familial psychiatric disorders. The comorbidity of ADHD and PBD increased the severity of ADHD problems, which is consistent with the results of

Table 1. Comparison Between ADHD Children With and Without PBD on Demographic Data, Cognitive Level, ADHD Symptomatology, and Comorbidity (Lifetime).

	ADHD with PBD	ADHD without PBD		
	<i>n</i> = 49	<i>n</i> = 320	χ^2/F	<i>p</i>
<i>M; SD</i>				
Age (years)	8.54; 2.46	8.80; 2.52	0.45	<i>ns</i>
SES	74.96; 17.00	74.82; 13.17	0.00	<i>ns</i>
IQ-Total	98.90; 11.83	99.93; 14.55	0.23	<i>ns</i>
IQ-Performance	96.63; 12.23	96.84; 14.59	0.01	<i>ns</i>
IQ-Verbal	101.88; 12.88	102.44; 14.95	0.06	<i>ns</i>
ADHD-RS Total score	40.65; 6.98	35.63; 10.20	9.64	.00
ADHD-RS Hyperactivity subscale	20.69; 3.86	17.48; 4.70	20.81	.00
ADHD-RS Inattentive subscale	19.39; 4.34	17.97; 4.51	4.25	.04
<i>n</i> (%)				
Boys	46 (94)	278 (87)	1.96	<i>ns</i>
Combined subtype	33 (67)	152 (48)	6.69	.01
Hyperactive subtype	8 (16)	42 (13)	0.37	<i>ns</i>
Inattentive subtype	8 (16)	126 (39)	9.76	.00
Anxiety disorders (generalized and separation anxiety disorders, phobias, panic disorder)	8 (16)	36 (11)	1.04	<i>ns</i>
Oppositional defiant disorder	34 (69)	102 (32)	25.52	.00
Conduct disorder	14 (29)	23 (7)	21.54	.00
Familial psychiatric disorders	24 (49)	22 (7)	8.73	.00

Note. PBD = pediatric bipolar disorder; SES = socioeconomic status; ADHD-RS = ADHD Rating Scale.

a previous study (Serrano et al., 2013). Specifically, our findings lead to the hypothesis that ADHD children with PBD are characterized by more disruptive and impulsive behaviors. However, our sample consists of selected outpatients of a specialized center for ADHD, and we could assume that the population which seeks medical attention from a specialized center showed severe symptoms. Further community-based studies are warranted to clarify this controversial topic.

Also consistent with prior studies (Donfrancesco et al., 2011), the combined subtype of ADHD was more frequent in children with PBD comorbidity than in those without PBD comorbidity, whereas the inattentive subtype was less frequent in children with PBD comorbidity.

Moreover, ADHD children with PBD showed higher percentage of other comorbid disorders, than the ADHD-alone group, including ODD and CD. No differences in rates of anxiety disorders were identified. Previous studies indicated that the comorbidity of PBD in ADHD is associated with greater comorbidity with anxiety, disruptive behavior disorders, and a psychopathological profile characterized by increased externalizing problems, anxious/depressed, social problems, and thought problems (Biederman et al., 1996; Diler et al., 2007; Donfrancesco et al., 2011; Mick, Biederman, Pandina, & Faraone, 2003). Recently, Serrano et al. (2013) in a sample of ADHD children with PBD found higher comorbidity with ODD and CD and a psychopathological profile characterized by

higher scores on the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001) scales of Rule-Breaking Behavior, Externalizing Problems, and Total Problems.

With regard to family history, the analysis revealed a higher number of familial psychiatric disorders in ADHD children with PBD than in children without PBD comorbidity. Data are consistent with previous studies, which revealed that the co-occurrence of psychiatric disorders is more likely in children with ADHD and comorbid disorders, such as oppositional defiant and CD (Pliszka, 2000) and PBD (Donfrancesco et al., 2011).

This study has several limitations. First, we evaluated a clinical and not a community-based sample, which means that only serious cases, that is, those most likely come to the attention of mental health services, were included. Second, the sample was collected in a single city in central Italy. A wider catchment area that included rural areas and was not limited to one city such as Rome would have lent more weight to our findings. Third, familial psychiatric disorders were studied only by an anamnestic method; a direct clinical assessment would be a better way to evaluate the real rates of psychopathology in family members, which in our study are divergent from previous literature.

A consequence of this limitation could be the low rate of parental psychopathology in ADHD without BD children.

In conclusion, the impact of early-onset BD on ADHD further clarifies the clinical relationship between these two diagnoses and their reciprocal influence.

In the assessment of ADHD children, attention must be paid to the identification of the PBD symptoms. Approximately 1 of 10 ADHD children may show this disorder, especially when ADHD symptoms are severe. The presence of PBD in ADHD children should alert clinicians to appropriate therapeutic strategies (pharmacological and psychological) that take into account not only the characteristics of ADHD symptoms but also mood alterations.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

- Achenbach, T. M., & Rescorla, L. A. (2001). *Manual for the ASEBA school-age forms and profiles*. Burlington: University of Vermont, Research Center for Children, Youth and Families.
- Barkley, R. A., & Murphy, K. R. (2006). *Attention deficit hyperactivity disorder: A clinical workbook*. New York, NY: Guilford Press.
- Biederman, J., Faraone, S., Mick, E., Wozniak, J., Chen, L., Ouellette, C., & Lelon, E. (1996). Attention-deficit hyperactivity disorder and juvenile mania: An overlooked comorbidity? *Journal of the American Academy of Child & Adolescent Psychiatry*, 35, 997-1008.
- Biederman, J., Makris, N., Valera, E. M., Monuteaux, M. C., Goldstein, J. M., Buka, S., . . . Seidman, L. J. (2008). Towards further understanding of the co-morbidity between attention deficit hyperactivity disorder and bipolar disorder: A MRI study of brain volumes. *Psychological Medicine*, 38, 1045-1056.
- Carlson, G. A. (2011). Broadening bipolar disorder—By design or accident? *World Psychiatry*, 3, 9-10.
- Chengappa, K. N., Kupfer, D. J., Frank, E., Houck, P. R., Grochocinski, V. J., Cluss, P. A., & Stapf, D. A. (2003). Relationship of birth cohort and early age at onset of illness in a bipolar disorder case registry. *American Journal of Psychiatry*, 160, 1636-1642.
- Diler, R. S., Uguz, S., Seydaoglu, G., Erol, N., & Avci, A. (2007). Differentiating bipolar disorder in Turkish prepubertal children with attention-deficit hyperactivity disorder. *Bipolar Disorders*, 9, 243-251.
- Donfrancesco, R., Marano, A., Innocenzi, M., Toni, L., Di Lelio, A., Milone, A. R., & DelBello, M. P. (2014). A comparison of bipolar disorders in children in Italy and the United States. *Journal of Affective Disorders*, 159, 53-55.
- Donfrancesco, R., Miano, S., Martinez, F., Ferrante, L., Melegari, M. G., & Masi, G. (2011). Bipolar disorder co-morbidity in children with attention deficit hyperactivity disorder. *Psychiatry Research*, 30, 333-337.
- Faraone, S. V., & Biederman, J. (1997). Do attention deficit hyperactivity disorder and major depression share familial risk factors? *Journal of Nervous and Mental Disease*, 185, 533-541.
- Galanter, C. A., & Leibenluft, E. (2008). Frontiers between attention deficit hyperactivity disorder and bipolar disorder. *Child and Adolescent Psychiatric Clinics of North America*, 17, 325-346.
- Geller, B., & DelBello, M. P. (2005). *Bipolar disorder in childhood and early adolescence*. New York, NY: Guilford Press.
- Geller, B., Sun, K., Zimmerman, B., Luby, J., Frazier, J., & Williams, M. (1995). Complex and rapid-cycling in bipolar children and adolescents: A preliminary study. *Journal of Affective Disorders*, 34, 259-268.
- Hassan, A., Agha, S. S., Langley, K., & Thapar, A. (2011). Prevalence of bipolar disorder in children and adolescents with attention-deficit hyperactivity disorder. *British Journal of Psychiatry*, 198, 195-198.
- Hollingshead, A. B. (1975). *Four Factor Index of Social Status*. New Haven, CT: Yale Press.
- Kaufman, J., Birmaher, B., Brent, D., Rao, U. M. A., Flynn, C., Moreci, P., & Ryan, N. (1997). Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (K-SADS-PL): Initial reliability and validity data. *Journal of the American Academy of Child & Adolescent Psychiatry*, 36, 980-988.
- Kennedy, N., Boydell, J., van Os, J., & Murray, R. M. (2004). Ethnic differences in first clinical presentation of bipolar disorder: Results from an epidemiological study. *Journal of Affective Disorders*, 83, 161-168.
- Kim, E. Y., & Miklowitz, D. J. (2002). Childhood mania, attention deficit hyperactivity disorder and conduct disorder: A critical review of diagnostic dilemmas. *Journal of Bipolar Disorders*, 4, 215-225.
- Kowatch, R. A., Fristad, M., Birmaher, B., Wagner, K. D., Findling, R. L., Hellander, M., & Child Psychiatric Workgroup on Bipolar Disorder. (2005). Treatment guidelines for children and adolescents with bipolar disorder (Abstract). *Journal of the American Academy of Child & Adolescent Psychiatry*, 44, 213-235.
- Luby, J., & Belden, A. (2006). Defining and validating bipolar disorder in the preschool period. *Development and Psychopathology*, 18, 971-988.
- Marzocchi, G. M., & Cornoldi, C. (2000). Una scala di facile uso per la rilevazione dei comportamenti problematici dei bambini con Deficit di Attenzione e Iperattività [An easy to use scale for the assessment of problematic behaviors of children with Attention Deficit Hyperactivity Disorder]. *Psicologia clinica dello sviluppo*, 4(1), 43-64.
- Masi, G., Perugi, G., Millepiedi, S., Mucci, M., Pfanner, C., Berloff, S., . . . Akiskal, H. S. (2010). Pharmacological response in juvenile bipolar disorder subtypes: A naturalistic retrospective examination. *Psychiatry Research*, 15, 192-198.
- Masi, G., Perugi, G., Millepiedi, S., Toni, C., Mucci, M., Bertini, N., & Akiskal, H. S. (2007). Clinical and research implications of panic-bipolar comorbidity in children and adolescents. *Psychiatry Research*, 153, 47-54.
- Masi, G., Perugi, G., Toni, C., Millepiedi, S., Mucci, M., Bertini, N., & Akiskal, H. S. (2004). Obsessive-compulsive bipolar

- comorbidity: Focus on children and adolescents. *Journal of Affective Disorders*, 78, 175-183.
- Masi, G., Perugi, G., Toni, C., Millepiedi, S., Mucci, M., Bertini, N., & Pfanner, C. (2006). Attention deficit hyperactivity disorder—Bipolar comorbidity in children and adolescents. *Bipolar Disorders*, 8, 373-381.
- Mick, E., Biederman, J., Pandina, G., & Faraone, S. V. (2003). A preliminary meta-analysis of the child behavior checklist in pediatric bipolar disorder. *Biological Psychiatry*, 53, 1021-1027.
- Milberger, S., Biederman, J., Faraone, S. V., Murphy, J., & Tsuang, M. T. (1995). Attention deficit hyperactivity disorder and comorbid disorders: Issues of overlapping symptoms. *American Journal of Psychiatry*, 152, 1793-1799.
- Miller, S., Chang, K. D., & Ketter, T. A. (2013). Bipolar disorder and attention deficit hyperactivity disorder comorbidity in children and adolescents: Evidence-based approach to diagnosis and treatment. *Clinical Psychiatry*, 74, 628-629.
- Molina, B. S., Hinshaw, S. P., Swanson, J. M., Arnold, L. E., Vitiello, B., Jensen, P. S., . . . MTA Cooperative Group. (2009). The MTA at 8 years: Prospective follow-up of children treated for combined-type ADHD in a multisite study. *Journal of the American Academy of Child & Adolescent Psychiatry*, 48, 484-500.
- Orsini, A., & Picone, L. (2006). *WISC-III: Contributo alla taratura italiana* [WISC-III: Italian validation]. Florence: Giunti OS Ed.
- Pataki, C., & Carlson, G. A. (2013). The comorbidity of ADHD and bipolar disorder: Any less confusion? *Current Psychiatry Reports*, 15, 372.
- Pliszka, S. R. (2000). Patterns of psychiatric comorbidity with attention-deficit/hyperactivity disorder. *Child and Adolescent Psychiatric Clinics of North America*, 9, 525-540.
- Sachs, G. S., Baldassano, C. F., Truman, C. J., & Guille, C. (2000). Comorbidity of attention deficit hyperactivity disorder with early- and late-onset bipolar disorder. *American Journal of Psychiatry*, 157, 466-468.
- Serrano, E., Ezpeleta, L., & Castro-Fornieles, J. (2013). Comorbidity and phenomenology of bipolar disorder in children with ADHD. *Journal of Attention Disorders*, 17, 330-338.
- Singh, M. K., DelBello, M. P., Kowatch, R. A., & Strakowski, S. M. (2006). Co-occurrence of bipolar and attention-deficit hyperactivity disorders in children. *Bipolar Disorders*, 8, 710-720.
- Soutullo, C. A., Canales, I. E., Wozniak, J., Garrán, P. G., Quintana, A. F., & Biederman, J. (2009). Pediatric bipolar disorder in a Spanish sample: Features before and at the time of diagnosis. *Journal of Affective Disorders*, 118, 39-47.
- Tamam, L., Karaku, G., & Ozpoyraz, N. (2008). Comorbidity of adult attention deficit hyperactivity disorder and bipolar disorder: Prevalence and clinical correlates. *European Archives of Psychiatry & Clinical Neuroscience*, 258, 385-393.
- Tillman, R., & Geller, B. (2006). Controlled study of switching from attention deficit/hyperactivity disorder to a prepubertal and early adolescent bipolar I disorder phenotype during 6-year prospective follow-up: Rate, risk, and predictors. *Developmental Psychopathology*, 18, 1037-1053.
- Tramontina, S., Schmitz, M., Polanczyk, G., & Rohde, L. A. (2003). Juvenile bipolar disorder in Brazil: Clinical and treatment findings. *Biological Psychiatry*, 53, 1043-1049.
- West, A. E., Schenkel, L. S., & Pavuluri, M. N. (2008). Early childhood temperament in pediatric bipolar disorder and attention deficit hyperactivity disorder. *Journal of Clinical Psychology*, 64, 402-421.
- Wilens, T. E., Biederman, J., Brown, S., Tanguay, S., Monuteaux, M. C., Blake, C., & Spencer, T. J. (2002). Psychiatric comorbidity and functioning in clinically referred preschool children and school-age youths with ADHD. *Journal of the American Academy of Child & Adolescent Psychiatry*, 41, 262-268.
- Wolf, D. V., & Wagner, K. D. (2003). Bipolar disorder in children and adolescents. *CNS Spectrums*, 8, 954-959.
- Wozniak, J. (2005). Recognizing and managing bipolar disorder in children. *Journal of Clinical Psychiatry*, 66, 18-23.
- Wozniak, J., Biederman, J., Kwon, A., Mick, E., Faraone, S., Orlowsky, K., & van Grondelle, A. (2005). How cardinal are cardinal symptoms in pediatric bipolar disorder? An examination of clinical correlates. *Biological Psychiatry*, 58, 583-588.

Author Biographies

Renato Donfrancesco, MD, obtained the degree from Pisa University in 1977. He is a specialist in pediatrics and in child neuropsychiatry. He works at S. Pertini Hospital of Rome as senior consultant in the Child Neuropsychiatry Department.

Michela Di Trani is a psychologist and psychotherapist. She has a PhD in dynamic, clinical, and developmental psychology and works in the Department of Dynamic and Clinical Psychology of Sapienza University of Rome.

Elda Andriola is a psychologist and cognitive-behavior psychotherapist. She is professor of psychodiagnostics in infancy and childhood at LUMSA University, Department of Human Sciences, Rome.

Daniela Leone is a child neuropsychiatrist and she is working toward a PhD in neuroscience at Catholic University of Sacro Cuore in Rome (Italy). She has been studying the biological basis and comorbidity of ADHD and mood disorder.

Maria G. Torrioli, MD, is a specialist in child neuropsychiatry. She is an associate professor at the Medicine Faculty of Sacro Cuore University of Rome.

Francesca Passarelli, MD, is a specialist in biology. She works as a researcher in the Department of Molecular Medicine at Sapienza University of Rome, where she is the chief of the Laboratory of Neurology and Immunology.

Melissa P. DelBello, MD, works as child and adolescent psychiatrist at the University of Cincinnati Medical Center and Cincinnati Children's Hospital Medical Center. She is the vice-chair of Clinical Research in the Division of Psychiatry, the director of Research Training and Education at Cincinnati Children's, and the co-director of the Division of Bipolar Disorders Research at the UC College of Medicine.