IN REVIEW

Anxiety Disorders in Children and Adolescents With Bipolar Disorder: A Neglected Comorbidity

Gabriele Masi, MD[1], Cristina Toni, MD[2], Giulio Perugi, MD[3], Maria Mucci, MD[4], Stefania Millepiedi, MD[5], Hagop S Akiskal, MD[6]

Objective: *We describe a consecutive clinical sample of children and adolescents with bipolar disorder to define the pattern of comorbid anxiety and externalizing disorders (attention-deficit hyperactivity disorder [ADHD] and conduct disorder [CD]) and to explore the possible influence of such a comorbidity on their cross-sectional and longitudinal clinical characteristics.*

Methods: *The sample comprised 43 outpatients, 26 boys and 17 girls, (mean age 14.9 years, SD 3.1; range 7 to 18), with bipolar disorder type I or II, according to DSM-IV diagnostic criteria. All patients were screened for psychiatric disorders using historical information and a clinical interview, the Diagnostic Interview for Children and Adolescents-Revised (DICA-R). To shed light on the possible influence of age at onset, we compared clinical features of subjects whose bipolar onset was prepubertal or in childhood (< 12 years) with those having adolescent onset. We also compared different subgroups with and without comorbid externalizing and anxiety disorders.*

Results: *Bipolar disorder type I was slightly more represented than type II (55.8% vs 44.2%). Only 11.6% of patients did not have any other psychiatric disorder; importantly, 10 subjects (23.5%) did not show any comorbid anxiety disorder. Comorbid externalizing disorders were present in 12 (27.9%) patients; such comorbidity was related to the childhood onset of bipolar disorder type II. Compared with other subjects, patients with comorbid anxiety disorders more often reported pharmacologic (hypo)mania.*

(Can J Psychiatry 2001;46:797–802)

Key Words: *bipolar disorder, externalizing disorders, anxiety disorders, pharmacologic hypomania*

In the past 2 decades, there has been increasing awareness that bipolar disorders begin in juvenile years (1–5), and since 1980 diagnostic criteria for bipolar disorder in adults have also been used to diagnose mania in children. Obstacles to identifying and diagnosing mania in children and adolescents essentially include the diversity in clinical presentation within and across episodes and the symptomatic overlap with externalizing disorders commonly found in childhood, such as attention-deficit hyperactivity disorder (ADHD) and conduct disorder (CD) (4, 6–8). There is consensus that uncomplicated classic manic-depressive illness is rare in children and that in the case of comorbidity with externalizing disorders, the question is whether these latter and bipolar disorder actually represent distinct illnesses (9,10).

Epidemiological data on bipolar disorder in juvenile subjects are scarce and conflicting. A community study of adolescents in the US reported a 0.99% prevalence rate of full-blown bipolar disorder (11); periods of abnormally persistent, elevated, expansive, or irritable mood were prevalent (5.7%), although they did not fulfill criteria for bipolar I, bipolar II, or cyclothymia (11). In another survey of adolescents, the prevalence of bipolar disorder varied from 0.6% to 13.3%, depending upon whether the duration and severity criteria were applied (12). There are no community studies of bipolar disorder in preteens.

Several predictors of bipolar disorder outcome in adolescents with major depression have been suggested: family history of bipolar disorder, sudden onset, presence of delusions, psychomotor retardation and hypersomnia, and

Manuscript received and accepted September 2001.

[1]Researcher, Division of Child Neurology and Psychiatry, University of Pisa, IRCCS Stella Maris, Calambrone, Pisa, Italy.
[2]Researcher, Department of Psychiatry, University of Pisa, and Institute of Behavioural Sciences, Carrara-Pisa, Italy.
[3]Researcher, Department of Psychiatry, University of Pisa, and Institute of Behavioural Sciences, Carrara-Pisa, Italy.
[4]Researcher, Division of Child Neurology and Psychiatry, University of Pisa, IRCCS Stella Maris, Calambrone, Pisa, Italy.
[5]Researcher, Division of Child Neurology and Psychiatry, University of Pisa, IRCCS Stella Maris, Calambrone, Pisa, Italy.
[6]Professor of Psychiatry and Director, International Mood Center, Department of Psychiatry at the University of California at San Diego and Veterans Administration Medical Center, La Jolla , California.
Address for correspondence: Dr Gabriele Masi, INPE–University of Pisa, Via dei Giacinti 2, 56018, Calambrone (Pisa) Italy
e-mail: masi@inpe.unipi.it

Table 1. Demographic and clinical features, lifetime comorbidity, and first-degree family history in children and adolescents with bipolar disorder (*n* = 43)

Age, mean (SD)	14.9 (3.1)
< 13 years, *n* (%)	20 (46.5)
From 13 to 18 years, *n* (%)	23 (53.9)
Sex	
Male subjects, *n* (%)	26 (60.5)
Female subjects, *n* (%)	17 (39.5)
Lifetime comorbidity, *n* (%)	
Obsessive–compulsive disorder	26 (44.2)
Social phobia	17 (39.5)
Panic disorder or agoraphobia	11 (25.6)
Separation anxiety disorder	7 (16.3)
Generalized anxiety disorder	8 (18.6)
Attention-deficit hyperactivity disorder or conduct disorder	12 (27.9)
Age at onset, mean (SD)	
Bipolar disorder	12.27 (2.94)
Obsessive–compulsive disorder	9.63 (2.71)
Social phobia	6.62 (1.74)
Panic disorder or agoraphobia	10.27 (4.62)
Separation anxiety	6.12 (2.69)
Generalized anxiety disorder	8.62 (1.99)
Attention-deficit hyperactivity disorder or conduct disorder	4.2 (0.63)
Comorbid anxiety disorders, mean (SD)	1.41(1.18)
None, *n* (%)	10 (23.5)
1	15 (34.9)
2 or more	18 (41.6)
Comorbid disorders, mean (SD)	1.81 (1.5)
None, *n* (%)	5 (11.6)
1	18 (41.9)
2 or more	20 (46.5)
CGI-Severity, mean (SD)	4.85 (0.78)

[a]CGI-Severity = Clinical Global Impression-Severity

pharmacologically induced (hypo)mania (13–15). Moreover, what seems unique to juvenile bipolar disorder is the almost invariable presence of other concomitant disorders. As in adults, comorbidity is the rule rather than the exception among children and adolescents with bipolar disorder. In particular, comorbidity with externalizing disorders has been widely reported, even if definitive conclusions have not been attained (4, 8–10). Other comorbidities, however, have also been observed, including anxiety disorders (11,7), drug and alcohol abuse (11,16), and eating and impulse-control disorders (11,17).

Although comorbidity with anxiety disorders appears as a clinically relevant phenomenon, it has not been studied as well as has comobidity with externalizing disorders. Akiskal and others reported that of the 44 offspring (aged 6 to 18 years old) of probands with bipolar disorder, 18.2% had initially received anxiety disorder diagnoses in an era when the latter were not even part of the official diagnostic practice (1). Bashir and others noted that concomitant anxiety disorders were present in 53% of adolescents with diagnosed mania or hypomania (18). In a representative community sample of 1709 adolescents (aged 14 to 18 years), 37 of 115 subjects (32.2%) meeting DSM-IV criteria for bipolar disorder or with subthreshold bipolar symptomatology were also found to meet criteria for specific anxiety disorders (11). In clinical studies of children with mania (12 years or younger), anxiety disorders were found in more than one-half of the cases (19,20). Similarly, Zahn-Waxler and others and Sachs and others both reported an increased risk for anxiety disorders in high-risk children of parents with bipolar disorder (21,22).

Our study describes a consecutive clinical sample of children and adolescents with bipolar disorder to define the pattern of comorbid anxiety and externalizing disorders and to explore the possible influence of such comorbidity on their cross-sectional and longitudinal clinical characteristics.

Methods

Sample

This was a naturalistic study based on a clinical database of 43 outpatients followed for a mean period of 17.56 months (range 1 to 48). All the subjects, aged between 7 and 20 years, were screened for psychiatric disorders, using historical information and a clinical interview, the Diagnostic Interview for Children and Adolescents-Revised (DICA-R) (23). We excluded all patients with schizophrenia or mental retardation, as well as those with poor verbal skills (expression or comprehension). These patients (26 male patients and 17 female patients; mean age 15.14 years, SD 3.39 years) were diagnosed with bipolar disorder (type I, *n* = 24, 55.8%; type II, *n* = 19, 44.2%) according to DSM-IV diagnostic criteria. The severity of the illness was recorded at baseline and thereafter monthly for a period up to 48 months.

Measures

The DICA-R was administered individually to the children and adolescents participating in the study and to their parents. The DICA-R is a structured interview using DSM-IV criteria and organized to explore the presence or absence of each symptom in different psychiatric syndromes. Three trained child psychiatrists administered the clinical interview. The subject's comprehension of the questions was carefully assessed; if necessary, questions were repeated to clarify the youngster's response. All participants in the study were considered competent to undergo the diagnostic interview. To reach consensus and improve the reliability and validity of their diagnosis, the research clinicians reviewed the clinical data from each subject–parent pair after each interview. When questions arose, patients and parents were reassessed for further clarification. Structured interview diagnoses were considered positive only if DSM-IV criteria were unequivocally met. Our previous analyses of children and adolescents assessed with DICA-R revealed a good interrater reliability

Table 2. Clinical features and lifetime comorbidity in childhood- and adolescent-onset bipolar disorder

	Childhood-onset	Adolescent-onset		
	n = 20	*n* = 23	χ^2	*P*
Age, mean (SD)	12.95 (3.4)	16.6 (1.3)	–4.73	0.0001
Age at onset, mean (SD)	9.85 (2.50)	14.39 (1.10)	–7.92	0.0001
Clinical global impression, mean (SD)	4.68 (0.759)	5 (0.80)	–1.31	ns
Bipolar disorder				
Type I, *n* (%)	8 (40.0)	16 (69.6)		
Type II, *n* (%)	12 (60.0)	7 (30.4)	3.79	0.051
Lifetime comorbidity, *n* (%)				
Obsessive–compulsive disorder	8 (40.0)	11 (47.8)	0.27	ns
Social phobia	8 (40.0)	9 (39.1)	0.003	ns
Panic disorder or agoraphobia	4 (20.0)	7 (30.4)	0.61	ns
Separation anxiety disorder	3 (15.0)	4 (17.4)	0.04	ns
Generalized anxiety disorder	4 (20.0)	4 (17.4)	0.048	ns
Attention-deficit hyperactivity disorder or conduct disorder	10 (50.0)	2 (8.7)	9.07	0.003
Comorbid anxiety disorders, mean (SD)	1.3 (1.4)	1.5 (1.0)	–0.61	ns
Comorbid disorders, mean (SD)	2.1 (1.87)	1.61 (1.12)	0.95	ns
Pharmacologic hypomania, *n* (%)	7 (35.0)	5 (21.74)	0.93	ns
Index episode, *n* (%)				
Depressive	11 (55.0)	7 (30.4)		
(Hypo)mania	3 (15.0)	11 (47.8)		
Mixed	6 (30.0)	5 (21.7)	5.37	ns (0.07)

for the diagnosis ($\kappa > 0.75$) (24). The severity of the illness at baseline and subsequent improvement during follow-up were assessed by means of the Clinical Global Impression (CGI).

Statistical Analyses

We used descriptive analyses. To shed light on the possible influence of age at onset on the clinical picture, we compared the clinical features of subjects whose bipolar disorder onset occurred during childhood with those having adolescent onset. With the aim of individualizing clinical characteristics related to comorbid externalizing or internalizing disorders, we also compared different subgroups with and without comorbidity. Chi-square analyses were performed on categorical variables and unpaired *t*-tests on continuous variables. Fisher's exact test and the Mann-Whitney U-test were used when appropriate. Statistical significance was conservatively set at 2-tailed 5% level ($P < 0.05$).

Results

In our sample, bipolar disorder type I was slightly more represented than type II ($n = 24$, 55.8% vs $n = 19$, 44.2%). As shown in Table 1, bipolar disorder mean age at onset was higher than that of anxiety disorders and externalizing disorders. Only a few patients did not have any other psychiatric disorder ($n = 5$, 11.6%); 10 (23.5%) did not show a comorbid anxiety disorder. Eighteen patients (41.9%) had more than 1 anxiety disorder. Obsessive–compulsive disorder (OCD) was the most prevalent (44.2%) anxiety disorder, followed by social phobia (SP) (39.5%) and panic disorder (PD) (25.6%). Separation anxiety (SA) (16.3%) and generalized anxiety disorder (GAD) (18.6%) were less frequently reported. ADHD and CD were present in about one-quarter of the sample (27.9%). At baseline, illness severity according the CGI-Severity score was 4.85 (SD 0.8), indicating moderate-to-severe illness.

After dividing the sample into 2 groups based on the onset of the bipolar disorder (during childhood [$n = 20$] or adolescence [$n = 23$]) (Table 2), we did not find significant relations between age at onset and clinical features such as illness severity or anxiety comorbidity; the only difference found concerns a statistically significant higher percentage of patients with comorbid externalizing disorders who reported childhood-onset bipolar disorder. Patients with comorbid externalizing disorders suffered from bipolar type II more often than those without externalizing comorbidity (Table 3). Focusing on the presence of anxiety disorders, we found that the patients with such comordidity more often reported pharmacologic (hypo)mania, compared with the others (Table 4).

Discussion

In our sample of children and adolescents with bipolar disorder, the comorbidity with anxiety disorders was very prevalent; only a few patients did not show any comorbid anxiety disorder. This finding is generally consistent with previous

Table 3. Clinical features and lifetime comorbidity in youths having bipolar disorder with and without externalizing disorders

	Externalizing	No externalizing		
	n = 12	*n* = 31	χ^2	*p*
Age, mean (SD)	12.6 (4.5)	15.8 (1.7)	–3.42	0.001
Age at onset, mean (SD)	9. 5 (3.48)	13.35 (1.85)	–4.72	0.0001
Clinical global impression, mean (SD)	4.67 (0.65)	4.93 (0.83)	–1.0	ns
Bipolar disorder				
Type I, *n* (%)	2 (16.7)	22 (71.0)		
Type II, *n* (%)	10 (83.3)	9 (29.0)	10.34	0.001
Lifetime comorbidity, *n* (%)				
Obsessive–compulsive disorder	4 (33.3)	15 (48.4)	0.79	ns
Social phobia	4 (33.3)	13 (41.9)	0.27	ns
Panic disorder or agoraphobia	2 (16.7)	9 (29.0)	0.69	ns
Separation anxiety disorder	2 (16.7)	5 (16.1)	0.002	ns
Generalized anxiety disorder	2 (16.7)	6 (19.3)	0.041	ns
Comorbid anxiety disorders, mean (SD)	1. 17 (1.19)	1.51 (1.18)	–0.87	ns
Pharmacologic hypomania, *n* (%)	3 (25.0)	9 (29.0)	0.07	ns
Index episode, *n* (%)				
Depressive	7 (58.3)	11 (35.5)		
(Hypo)mania	1 (8.3)	13 (41.9)		
Mixed	4 (33.3)	7 (22.6)	4.47	ns

Table 4. Clinical features in youths having bipolar disorder with and without anxiety comorbidity

	Anxiety	No anxiety		
	n = 33	*n* = 10	χ^2	*P*
Age, mean (SD)	14.7 (4.4)	15.0 (2.7)	0.24	ns
Age at onset, mean (SD)	12.6 (2.7)	11.1 (3.6)	–1.46	ns
Clinical global impression, mean (SD)	4.79 (0.78)	5.11 (0.78)	1.1	ns
Bipolar disorder				
Type I, *n* (%)	19 (57.6)	5 (50.0)		
Type II, *n* (%)	14 (42.4)	5 (50.0)	0.18	ns
Lifetime comorbidity, *n* (%)				
Attention-deficit hyperactivity disorder or conduct disorder	7 (21.2)	5 (50.0)	3.16	ns
Pharmacologic hypomania, *n* (%)	12 (36.4)	0 (0.0)	5.04	0.02
Index episode, *n* (%)				
Depressive	15 (45.4)	3 (30.0)		
(Hypo)mania	10 (30.3)	4 (40.0)		
Mixed	8 (24.2)	3 (30.0)	0.76	ns

reports in the literature (12,21,22,7,19,20). Even though bipolar disorder comorbidity with externalizing disorders has been studied much more frequently than its comorbidity with anxiety disorders, our data suggest that the latter are more represented. In addition, anxiety disorders like ADHD and CD antedated bipolar disorder. This might explain Akiskal and others' chart-review finding that the juvenile offspring of probands with bipolar disorder often initially receive anxiety disorder diagnoses, among others (1). This is likely in subjects with the internalizing or anxious depressive phase of bipolar disorder. Those in the externalizing phase might be initially diagnosed with ADHD or CD and, in extreme cases of psychosis, be diagnosed with schizophrenia (1).

As in previous work (4,25) dividing the sample based on onset of bipolar disorder during either childhood or adolescence, we found that comorbid ADHD and CD were associated with childhood onset. This finding suggests that a subform of ADHD may be a developmental marker for a very early-onset form of bipolar disorder. Recently, it has been suggested that hyperactivity is the first developmentally age-specific manifestation of prepubertal-onset bipolar disorder (26). The high rate of comorbid anxiety disorders with onset preceding bipolar disorder indicates that anxious

comorbidity should be subject to the same considerations. Hypothetically, if hyperactivity and CD might reflect an angry (hypo)manic behavioural equivalent, we submit that anxiety disorders might replace or coexist with bipolar depressive inhibition.

A comparison with adult anxious-bipolar comorbidity might provide a perspective to understand the foregoing hypothetical formulation. Frequent comorbidity between mood and anxiety disorders in adults has been widely reported in clinical (27–29) and epidemiological studies (30–32). In the Pisa–San Diego collaborative studies, we have investigated lifetime comorbidity between PD, SP, and OCD on the one hand and mood disorder on the other (27–29). Different temporal relations seemed to characterize the occurrence of (hypo)mania in individual anxiety disorder subtypes (29). Usually, SP chronologically preceded (hypo)manic episodes and disappeared when the latter episodes supervened. By contrast, PD and OCD often persisted during such episodes, even when they preceded them. Therefore, in some patients SP might lie on a broad affective continuum of inhibitory restraint vs disinhibited hypomania. Indeed, Himmelhoch hypothesized that SP might actually belong, in at least a significant minority of cases, to a bipolar spectrum (33).

As expected, in this study, the patients with bipolar disorder and anxiety disorders more often reported pharmacologic (hypo)mania, compared with those without this comorbidity. Several case reports describe antidepressant-associated (hypo)mania in children and adolescents with anxiety and depressive disorders (34–36), suggesting the need to be cautious when considering antidepressant pharmacotherapy in youths with severe, multiple anxiety disorders. To clarify the relations between anxiety and bipolar disorder, their chronological sequence should be studied thoroughly over long periods of time, with both retrospective and prospective inquiries. Apart from theoretical issues, therapeutic implications should encourage such analyses.

In a study of offspring of patients with bipolar disorder, Akiskal and others did not find full-blown mania before puberty (1). Also, reporting on the offspring of adults with classic bipolar disorder, Duffy and others found preponderantly classic bipolar disorder that almost always began postpubertally (5). The present analyses do not permit us to examine this question. It is likely, however, that our findings are relevant to the broad spectrum of bipolarity proposed by Akiskal (37).

Our results should be interpreted in light of specific methodological limitations. The poor reliability of both children's and parents' recall of previous episodes could have biased our findings. Moreover, many children with mania may have had early bipolar symptoms that could easily have led to an incorrect diagnosis of ADHD or CD. Structured diagnostic interview techniques can minimize informant and clinician bias and may be an improvement over the standard clinical assessment used in this study. Given the relative reluctance to diagnose bipolar disorder in young subjects, structured interviews provide a means of identifying cases that might otherwise be misattributed. However, observations made over long periods of time by clinicians who know their patients well provide an important validation.

Clinidal Implications

- Comorbidity with anxiety disorder is very common in a clinical population of children and adolescents with bipolar disorder.
- Frequent pharmacologic hypomania indicates the need to be cautious when considering antidepressant pharmacotherapy in juvenile subjects with multiple anxiety disorders.
- Juvenile anxious bipolarity might constitute a putative phenotype within the genetic spectrum of bipolar disorder.

Limitations

- This was a retrospective evaluation of lifetime comorbidity,
- Reliability of both children's and parents' recall of previous episodes was poor.
- Early bipolar disorder symptoms could be misinterpreted as attention-deficit hyperactivity disorder (ADHD) or conduct disorder (CD).

Globally, our findings suggest that the presence of anxiety disorders may be a hitherto-neglected characteristic of juvenile-onset bipolar disorders, overshadowed by the literature's emphasis on the externalizing aspects of bipolarity. Clearly, more work is needed to further understand the overlap between anxiety and mood disorders during childhood and adolescence. That pharmacologic (hypo)mania is prevalent in this population already underscores the clinical significance of anxious bipolarity in children. Moreover, such comorbidity could serve as a putative bipolar phenotype, relevant for future genetic investigations.

References

1. Akiskal HS, Downs J, Jordan P. Affective disorders in referred children and younger siblings of manic-depressives: mode of onset and prospective course. Arch Gen Psychiatry 1985;42:996–1003.
2. Weller RA, Weller EB, Tucker SG, Fristad MA. Mania in prepubertal children: has it been underdiagnosed? J Affect Disord 1986;11:151–4.
3. Geller B, Fox LW, Clark K. Rate and predictors of prepubertal bipolarity during follow up of 6-to-12 year-old depressed children. J Am Acad Child Adolesc Psychiatry 1994;33:461–8.
4. Biederman J, Faraone S, Mick E, Lelon E. Psychiatric comorbidity among referred juveniles with major depression: fact or artifact? J Am Acad Child Adolesc Psychiatry 1995;34:579–90.
5. Duffy A, Alda M, Kutcher S, Fusee C, Grof P. Psychiatric symptoms and syndromes among adolescent children of parents with lithium-responsive or lithium-nonresponsive bipolar disorder. Am J Psychiatry 1998;155:431–3.
6. Bowring MA, Kovacs M. Difficulties in diagnosing manic disorders among children and adolescents. J Am Acad Child Adolesc Psychiatry 1992;31:611–4.
7. Faraone SV, Biederman J, Wozniak J, Mundy E, Mennin D, O'Donnell D. Is comorbidity with ADHD a marker for juvenile-onset mania? J Am Child Adolesc Psychiatry 1997;36:1046–55.
8. Biederman J, Faraone SV, Chu MP, Wozniak J. Further evidence of a bi-directional overlap between juvenile mania and conduct disorder in children. J Am Acad Child Adolesc Psychiatry 1999;38:468–76.
9. Klein RG, Pine DS, Klein DF. Resolved: mania is mistaken for ADHD in prepubertal children–negative. J Am Acad Child Adolesc Psychiatry 1998;37:1093–6.

10. Biederman J. Resolved: mania is mistaken for ADHD in prepubertal children–affirmative. J Am Acad Child Adolesc Psychiatry 1998; 37:1091–3.
11. Lewinshon PM, Klein DN, Seeley JR. Bipolar disorder in community sample of older adolescents: prevalence, phenomenology, comorbidity and course. J Am Acad Child Adolesc Psychiatry 1995;34:454–63.
12. Carlson GA, Kashani JH. Manic symptoms in a non-referred adolescent population. J Affect Disord 1988;15:219–26.
13. Strober M, Carlson G. Bipolar illness in adolescents with major depression: clinical genetic, and psychopharmacologic predictors in a three- to four-year prospective follow-up investigation. Arch Gen Psychiatry 1982;39:549–55.
14. Akiskal HS, Walker P, Puzantian VR, King D, Rosenthal TL, Dranon M. Bipolar outcome in the course of depressive illness: phenomenologic, familial and pharmacologic predictors. J Affective Disord 1983;5:115–28.
15. Akiskal HS. Developmental pathways to bipolarity: are juvenile-onset depressions pre-bipolar? J Am Acad Child Adolesc Psychiatry 1995;34:754–63.
16. Rasanen P, Tiihonen J, Hakko H. The incidence and onset-age of hospitalized bipolar affective disorder in Finland. J Affect Disord 1998;48:63–8.
17. Kafantaris V, Coletti DJ, Dicker R, Padula G, Pollack S. Are childhood psychiatric histories of bipolar adolescents associated with family history, psychosis and response to lithium treatment? J Affect Disord 1998;51:153–64.
18. Bashir M, Russell J, Johnson G. Bipolar affective disorder in adolescence: a 10-year study. Aust N Z J Psychiatry 1987;21:36–43.
19. Wozniak J, Biederman J, Mundy E, Mennin D, Faraone SV. A pilot family study of childhood-onset mania. J Am Acad Child Adolesc Psychiatry 1995;34:1577–83.
20. Wozniak J, Biederman J, Faraone SV, Frazier J, Kim J, Millstein R, and others. Mania in children with pervasive developmental disorder revisited. J Am Acad Child Adolesc Psychiatry 1997;36:1552–60.
21. Zahn-Waxler C, Mayfield A, Radke-Yarrow M, McKnew D, Cytryn L, Davenport Y. A follow-up investigation of offspring of parents with bipolar disorder. Am J Psychiatry 1988;145:506–9.
22. Sachs GS, Conklin A, Lafer B, Thibault AB, Rosenbaum JF, Biederman J. Psychopathology in children of late vs early onset bipolar probands. Presented at the Proceedings of the Annual Meeting of the American Academy of Child and Adolescent Psychiatry 1993; San Antonio (TX).
23. Reich W. Diagnostic interview for children and adolescents revised DSM-IV version. Toronto (ON): Multi-Health Systems; 1997.
24. Masi G, Favilla L, Mucci M, Poli P, Romano R. Depressive symptoms in children and adolescents with dysthymic disorder. Psychopathology 2001;34:29–35.
25. Biederman J, Faraone SV, Hatch M, Mennin D, Taylor A, George P. Conduct disorder with and without mania in referred sample of ADHD children. J Affect Disord 1997;44:177–88.
26. Geller B, Luby J. Child and adolescent bipolar disorder: a review of the past 10 years. J Am Acad Child Adolesc Psychiatry 1997;36:1168–76.
27. Perugi G, Toni C, Akiskal HS. Anxious-bipolar comorbidity: diagnostic and treatment challenges. The Psychiatric Clinics of North America 1999;22:565–83.
28. Perugi G, Akiskal HS, Ramacciotti S, Nassini S, Toni C, Milanfranchi A, and others. Depressive comorbidity of panic, social phobic and obsessive-compulsive disorders re-examined: is there a bipolar connection? J Psychiatr Res 1999;33:53–61.
29. Perugi G, Akiskal HS, Toni C, Simonini E, Gemignani A. The temporal relationship between anxiety disorders and (hypo)mania: a retrospective examination of 63 panic, social phobic and obsessive-compulsive patients with comorbid bipolar disorder. J Affect Disord (Forthcoming).
30. Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, and others. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the national comorbidity survey. Arch Gen Psychiatry 1994;51:8–19.
31. Chen YW, Dilsaver SC. Comorbidity for obsessive-compulsive disorder in bipolar and unipolar disorders. Psychiatric Res 1995;59:57–64.
32. Angst J. The emerging epidemiology of hypomania and bipolar II disorder. J Affect Disord 1998;50:143–51.
33. Himmelhoch JM. Social anxiety, hypomania and the bipolar spectrum: data, theory and clinical issues. J Affect Disord 1998;50:203–13.
34. Geller B, Fox LW, Fletcher M. Effect of tryciclic antidepressants on switching to mania and on the onset of bipolarity in depressed 6- to 12- years-olds. J Am Acad Child Adolesc Psychiatry 1993;32(1):43–50.
35. Go F, Malley EE, Birmaher B, Rosenberg D. Manic behaviors associated with fluoxetine in three 12- to 18- year-olds with obsessive-compulsive disorder J Child Adolesc Psychopharmacol 1998;8(1):73–80.
36. Strober M. Mixed mania associated with tryicyclic antidepressant therapy in prepubertal delusional depression: three cases. J Child Adolesc Psychopharmacol 1988;8:181–5.
37. Akiskal HS. The prevalent clinical spectrum of bipolar disorders: beyond DSM-IV. J Clin Psychopharmacol 1996;17:117–22.

Résumé: Les troubles anxieux chez les enfants et les adolescents souffrant du trouble bipolaire sélectionnés de façon consécutive : une comorbidité négligée

Objectif : *Nous décrivons un échantillon clinique consécutif d'enfants et d'adolescents souffrant du trouble bipolaire pour définir le modèle de comorbidité des troubles anxieux et d'expression [trouble d'hyperactivité avec déficit de l'attention (THADA) et trouble des conduites (TC)] et sonder l'influence possible de cette comorbidité sur leurs caractéristiques cliniques croisées et longitudinales.*

Méthodes : *L'échantillon comprenait 43 patients externes, 26 garçons et 17 filles (moyenne d'âge 14,9 ans, écart-type 3,1; de 7 à 18 ans), de type bipolaire I ou II, selon les critères diagnostiques du* DSM-IV. *Les troubles psychiatriques ont été dépistés chez tous les patients à l'aide d'information sur les antécédents et d'une entrevue clinique, l'entrevue diagnostique révisée pour enfants et adolescents (DICA-R). Pour faire la lumière sur l'influence possible de l'âge où apparaît la maladie, nous avons comparé les traits cliniques des sujets chez qui le trouble bipolaire est apparu à la pré-puberté ou durant l'enfance (12 ans) avec ceux où l'apparition a eu lieu à l'adolescence. Nous avons également comparé différents sous-groupes avec et sans troubles anxieux ou d'expression comorbides.*

Résultats : *Le trouble bipolaire de type I était légèrement plus représenté que celui de type II (55,8 % et 44,2 %). Seulement 11,6 % des patients ne présentaient aucun autre trouble psychiatrique; notablement, 10 sujets (23,5 %) n'avaient aucun trouble anxieux comorbide. Les troubles d'expression comorbides étaient présents chez 12 patients (27,9 %); cette comorbidité était reliée à l'apparition dans l'enfance du trouble bipolaire de type II. Comparativement à d'autres sujets, les patients souffrant de troubles anxieux comorbides déclaraient plus souvent une (hypo)manie pharmacologique.*