

# Bipolar Disorder in Children and Adolescents: Current Challenges

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**Objective:** To demonstrate the diagnostic and treatment challenges in juvenile-onset bipolar disorder.

**Method:** Three case vignettes are outlined to demonstrate different bipolar presentations in children and adolescents.

**Results:** These case examples illustrate important issues in the diagnosis and management of juvenile-onset bipolar disorder. These issues include diagnostic confusion with atypical initial presentation and the effect of developmental factors on symptom expression. The relationship among genetic risk, early affective instability, and the stress generated by affectively ill family members is complex and circular. Comorbidity with disruptive behaviour disorders, as well as anxiety disorders, is demonstrated by the cases discussed. Comorbid disorders may affect outcome and require separate treatment intervention. There is evidence for the prophylactic antimanic effect of lithium carbonate in children and adolescents, but its specificity as an antimanic agent is still uncertain. There is less evidence, at present, for effectiveness of other mood stabilizers in this age group, although sodium valproate may prove more effective in mixed mania and rapid cycling, which are so often seen with early-onset bipolar disorder.

**Conclusions:** While the existence of juvenile-onset bipolar disorder is no longer in dispute, several outstanding issues related to diagnosis and long-term management remain. Careful prospective research will be necessary to sort out these issues definitively.

(Can J Psychiatry 1997;42:632–636)

**Key Words:** juvenile onset, bipolar disorder, atypical presentation, comorbidity, affective instability, treatment challenges

The conception that bipolar disorder or manic–depressive illness can occur in childhood and adolescence has only recently been accepted, and some authors even suggest that it may be underdiagnosed, especially in prepubertal children (1). Some of the difficulties in diagnosing bipolar disorder in young children are atypical presentation, developmental influences, and comorbidity, especially with externalizing disorders.

It has been suggested that early-onset manic–depressive illness may have a more chronic outcome, including a high incidence of suicide and frequently recurring mood swings with uncontrollable fluctuations in affective state (2,3). Inadequate treatment may deny a child or adolescent effective prophylaxis against future episodes and protection against ensuing complications, such as substance abuse, conduct disorder, or suicidal behaviour (4). In spite of these pressing dangers, our current knowledge about treating bipolar disorder in this age group is still limited.

The following vignettes, diagnosed by using DSM-IV (5) criteria, are presented to exemplify some of the challenges facing clinicians who diagnose and treat children and adolescents with bipolar disorder.

## Case A

This male child presented initially at 7 years old with anxiety symptoms manifest as school refusal, social avoidance, and panic, as well as escalating verbal and physical aggression on exposure to unfamiliar persons and places. This

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Manuscript received January 1997, revised and accepted May 1997.

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child had been difficult from birth and was described as a hyperactive toddler; by age 3, he began to show shyness of people, and 6 months later he developed moderately severe asthma. The paternal grandfather had always been a socially avoidant man given to explosiveness and had been hospitalized for a suicide attempt. A was placed on imipramine 25 mg twice daily at age 7, and following a school reintegration plan, he was able to have 2 years of more stable function, although he continued to be very demanding in his relationships.

He presented again at age 11 in the emergency room because of uncontrollable physical aggression. Over the preceding year his behavioural outbursts had again escalated and would occur with the slightest provocation. These outbursts now had an episodic pattern, lasting days to a few weeks, with intervening periods during which he was calm. He was having rapid mood changes and both initial and terminal insomnia. He was started on lithium carbonate and a small dose of thioridazine (10 mg twice daily) to modulate his mood and explosive outbursts.

Nine months later, he developed a flu-like illness early in the school year and was unable to return to school when the physical symptoms subsided. He described depressive symptoms, was started on clomipramine, and was reintegrated to school following a brief hospitalization. He has remained stable and euthymic on lithium carbonate 900 mg/day and clomipramine 50 mg/day, both in divided doses. He was given a DSM-IV diagnosis of bipolar disorder type I.

### Case B

This patient, an only child, presented at age 11 with irritable but labile mood and physical aggression. He was both paranoid (concerned about being poisoned) and grandiose (convinced he was famous) but described mood-incongruent auditory hallucinations. His affect was variable, ranging from blunted to inappropriate to euphoric, and his judgement and insight were limited. He had no thought insertion, withdrawal, or broadcasting, and no ideas of reference. He would frequently make grossly inappropriate comments (often of a sexual nature) and had difficulty engaging with peers. He had initial insomnia, poor concentration, and high energy.

Behavioural and academic difficulties had become evident when this boy started school. At age 7, a child psychiatrist diagnosed the patient as suffering from mild attention-deficit hyperactivity disorder (ADHD). The patient's mother had systemic lupus erythematosus and learning problems. His father had problems with reading and writing, but there was no known family psychiatric history.

This patient was hospitalized and was initially treated with thioridazine. He became overly sedated, however, and subsequently received risperidone 0.5 mg twice daily, which made him more manageable, although he continued to be disinhibited and affectively labile. Lithium carbonate was

added, following which he made significant and steady progress but continued to have a blunted affect and to relate interpersonally in an odd way. At discharge, he took 300 mg lithium carbonate in the morning and 600 mg at night in addition to his risperidone. His DSM-IV discharge diagnosis was schizoaffective disorder.

He was hospitalized again several months later with irritability and physical aggression. His mood was labile, with depressive and euphoric shifts, and his thinking grandiose. At that time, the mood component of his disorder was predominant, and it has continued to be so, resulting in a change in diagnosis to bipolar disorder type I.

### Case C

This 8-year-old girl was hospitalized on an urgent basis because she exhibited a wide range of intense emotions, including extreme anger, intense sobbing, and regressed, baby-like play. In addition, she was often out of control at home, showing dramatic mood swings, anxiety, low frustration tolerance, and multiple somatic complaints. There was a strong history of psychiatric illness and mood disorder on both sides of the family.

Evidence of difficulties emerged around age 5 when her mother was pregnant with her younger brother, who developed a chronic physical ailment early in his infancy. Oppositional, anxious, and socially inappropriate behaviours intensified with the sibling's birth. These emotional and behavioural difficulties were evident at school, where she functioned poorly in her relationships with peers and adults. Her school teacher expressed concern that she had "given up on life."

At age 6, methylphenidate was prescribed by a pediatrician who had diagnosed ADHD because of her hyperactivity. There was no significant change, and fluoxetine was added to the methylphenidate with a striking deterioration in the child's behaviour; her speech became rapid, her activity level increased, and she engaged in dangerous behaviours, for example, cutting her forehead with a razor blade.

A diagnosis of bipolar disorder type II was made with the consideration of an episode of pharmacologically induced hypomania. She has remained stable on a combination of sodium valproate (125 mg twice daily) and risperidone (0.5 mg/day).

### Discussion

In the case examples outlined, each child presented pre-morbidity with hyperactivity as a symptom, but only one had a diagnosis of ADHD. As frequently occurs with juvenile-onset bipolar disorder, the clinical pictures in cases A and B were initially atypical, only with the passage of time did each

develop more discrete cyclical episodes and typical mood and behavioural changes.

In addition to the atypical initial presentation, these cases raise several other important issues. These include the colouring of symptom presentation by developmental factors and comorbid disorders; the consideration of latent bipolarity in children with affective instability and family history of mood disorder; treatment parameters for an index episode; the dilemmas of maintenance treatment; as well as the choices of mood-stabilizing agent. Each of these issues will be discussed separately.

### **Atypical Initial Presentation**

The diagnostic confusion with atypical presentations relates in part to the symptomatology in this age group. While it has long been observed that a change in mood is the presenting complaint in most young patients (6), the presence of a higher incidence of schizophreniform symptoms and significantly more delusions and ideas of reference has also been reported in manic patients under the age of 21 years (7). This point is well illustrated with case B, who initially received a diagnosis of schizoaffective disorder because of his atypical constellation of symptoms, including paranoid delusions, loosening of associations, blunted and inappropriate affect, and mood-incongruent auditory hallucinations. Over time, his manic and depressive symptoms became more prominent, the hallucinations were no longer evident, and he displayed euthymic mood.

Diagnostic accuracy with atypical presentation has important treatment implications. Carlson has pointed out how the psychotic episodes in some youth, diagnosed as schizophrenia, came to resemble typical bipolar disorder over time and how these youth responded to mood stabilizers with the same effectiveness as children with more obvious bipolar illness (8).

### **Developmental Factors and Comorbidity**

Major confounding factors of bipolar disorder in childhood and early adolescence are the influence of developmental factors and the presence of comorbid diagnoses. This may lead to both over- and underdiagnosis of bipolar disorder.

The clinical literature, both single case reports and case series, has noted an association between early-onset hyperactivity, disruptive and explosive behaviours, and bipolar disorder in childhood and adolescence (9–12). Winokur and others (13) indicated that bipolar adults and their adult bipolar relatives were more likely to have had a childhood history of hyperactivity than were unipolar subjects and their relatives. Comorbidity has also been found between conduct disorder and bipolar disorder in adolescents (14,15). Although the studies are fewer, an association between anxiety disorders and bipolar disorder in children and adolescents has also been

shown (16), and an increased risk for anxiety in children of bipolar parents has been described (17).

It is challenging to disentangle the relationship between these disorders aside from the impact of developmental factors on symptom expression. It may be that early-onset bipolar disorder is comorbid with other disorders, including multiple anxiety disorders, conduct disorder, oppositional defiant disorder, and ADHD (18). ADHD children with bipolar disorder have higher rates of psychopathology, psychiatric hospitalization, and severely impaired psychosocial functioning than other ADHD children (15). Early onset may also represent a more severe form of the disorder because of its impact on development: in addition, the diagnosis may be obscured by antisocial and impulsive behaviour, poor academic performance, and social withdrawal (19).

All cases demonstrate this range of early psychopathology, including behaviour problems and symptoms of early “hyperactivity.” It was not until they had more discrete episodes of mood change and inappropriate behaviour that the diagnosis of bipolar disorder was made. While the use of mood stabilizers may positively affect the outcome for these youth, the comorbid disorder may in itself affect prognosis quite apart from the mood disorder. Also, treatment strategies for a particular comorbid disorder may differ from the management of the mood disorder.

### **Affective Instability and Latent Bipolar Disorder**

Case C most clearly demonstrates the profile of the child demonstrating early affective instability in a family background loaded with mood disorder. Akiskal (20) has postulated that temperamental dysregulation provides the developmental substrate from which affective episodes arise. The proposed direction of causality, from temperament to stressors to affective episodes, provides one possible explanation for the deterioration of this child following the birth of her physically ill sibling. The situation was compounded by the precipitation of an affective episode in her biological father. The genetic risk for children born into families at risk for mood disorder is accentuated by the stress generated by individual affectively ill family members (21).

In a similar vein, affective instability was evident at an early age in case A, with emergence of anxiety symptoms at age 3 followed by school entry, maternal ill health, and parental separation. It was not until early adolescence that discrete and cyclical mood changes became evident.

### **Treatment Dilemmas in Juvenile Bipolar Disorder**

Although the first report of lithium use in the younger age group appeared in 1959 by VanKrevelen and Van Voorst, who described the successful treatment of a 14-year-old boy with “periodic psychosis” (22), there are still no controlled studies with ample sample size to demonstrate the efficacy of

lithium (or any other treatments) in bipolar children and adolescents (4).

While demonstrated lithium efficacy in adults (both in acute mania and prophylaxis) cannot be extrapolated to children and adolescents (4), 2 small sample size, placebo crossover studies (23,24) and 2 large open-treatment studies (25,26) suggest that, overall, lithium is beneficial in juvenile bipolar disorder. Significantly, the response rate in those under the age of 12 years who also have another Axis I disorder is considerably less than in those who first exhibited psychiatric symptoms in adolescence (40% versus 80%) (27).

Comorbidity with personality disorder has also been associated with decreased effectiveness of lithium in adolescents and increased likelihood of postdischarge neuroleptics (28). Severity of illness, which may have accounted for the difference, was not assessed, however.

A factor that needs to be considered in assessing the effectiveness of lithium treatment, particularly in a crossover design placebo–drug trial, is the negative effect of abrupt lithium withdrawal (29). This becomes important in maintenance treatment with lithium because the individual would require aggressive and longer-term use of lithium. The National Institute of Mental Health/National Institute of Health (NIMH/NIH) Consensus Development Panel on mood disorders did not establish criteria for prophylactic use of lithium in children and adolescents, and preventive use of lithium is based on clinical judgement (30). While there is a paucity of scientific evidence for the effectiveness of lithium prophylaxis in children and adolescents, 37 bipolar adolescents, stable on lithium, were followed up over 18 months in a naturalistic study (31). Thirty-five percent of the group were no longer compliant with lithium, and they had a 92.3% relapse rate compared with a relapse rate of 37.5% in those who remained compliant. The latter rate is similar to the 33% failure rate in adults (32). One of the challenges in sorting out lithium responsiveness has been the investigation of lithium in children and adolescents with heterogeneous disorders (25,32–35), including children with severe aggression directed toward self or others, children with bipolar or similar disorders, and behaviourally disturbed children whose parents have been lithium responsive. The specificity of lithium as an antimanic agent remains unclear; it may serve a “broad spectrum” function in dampening disruptive and explosive behaviours.

Other antimanic agents, including carbamazepine and sodium valproate, have been even less well studied in children and adolescents with psychiatric disorders. It has been suggested that anticonvulsants may be more effective than lithium in mixed mania and rapid cycling (36). Sodium valproate has also been used in conjunction with other medications (37,38).

Two of the 3 cases were treated with lithium, and there was an initial response. All the cases presented, however, required concomitant drug interventions to target nonbipolar symptoms.

## Conclusions and Recommendations

While the existence of bipolar disorder with onset in childhood and adolescence is no longer in doubt, issues of diagnostic accuracy and long-term management still lack clarity. In addition to factors of comorbidity, developmental influence on symptoms, and variable initial presentation, the underdiagnosis of the disorder in this age group makes systematic study difficult (39). Large-scale studies of clinical populations with longitudinal follow-up, as well as prospective studies of the at-risk offspring of bipolar parents, are needed to provide answers to these questions.

Clinicians need to consider the diagnosis of juvenile-onset bipolar disorder when they are presented with an atypical psychosis in adolescence, for example, in the affectively labile child with a family history of affective illness, especially bipolar disorder, and in volatile behaviour disorders with a marked mood component. Caution should be exercised about overdiagnosing bipolar disorder in disruptive behaviour disorders, however, because the decision to use mood-stabilizing drugs is a major step given the need for long-term maintenance and the presently unknown effects of long-term maintenance beginning in childhood.

In the case of presentation of typical bipolar disorder, monotherapy with a mood stabilizer is generally effective. Maintenance therapy is essential and should be long-term with regular monitoring. With the more complex juvenile presentations, treatment of comorbid disorders will necessitate the use of other psychotropic drugs in combination with a mood stabilizer and psychosocial support, although more research is needed with this population.

### Clinical Implications

- Clinicians need to be aware of the various presentations of juvenile-onset bipolar disorder.
- Understanding the developmental effects on symptom presentation in mood disorders will assist the clinician with diagnosis.
- While caution should be exercised in not overdiagnosing juvenile-onset bipolar disorder, recognition of the disorder and effective use of mood stabilizers may result in better outcomes.
- Comorbid disorders will require specific interventions.

### Limitations

- This is a clinical case study.
- Longitudinal research with well-defined case groups and children at risk for affective illness will be necessary to provide definitive answers to the issues raised in this paper.

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## Résumé

**Objectif :** Illustrer les défis relatifs au diagnostic et au traitement du trouble bipolaire juvénile.

**Méthode :** Trois vignettes de cas sont décrites afin d'illustrer diverses manifestations bipolaires chez les enfants et les adolescents.

**Résultats :** En se référant aux exemples de cas, on discute de questions comme les manifestations atypiques, l'incidence sur le développement, la comorbidité, la relation entre l'instabilité affective et le trouble bipolaire, ainsi que les défis relatifs au traitement dans ce groupe d'âge.

**Conclusions :** Même si on ne doute plus de l'existence du trouble bipolaire juvénile, plusieurs questions restent à régler en ce qui concerne le diagnostic et le traitement de longue durée. Il faudra mener des recherches prospectives minutieuses afin d'éclaircir ces questions une fois pour toutes.