The Public Health Aspects of Bipolar Disorder in Children and Adolescents

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Current Psychiatry Reports 2007, **9:**106–113
Current Medicine Group LLC ISSN 1523-3812

Bipolar disorder in children and adolescents is a major public health problem associated with significant functional impairment. Similar to adults with bipolar disorder, children and adolescents are at increased risk for substance-related disorders, weight problems, and impaired social support systems. Substance-related problems complicate treatment course. They often follow the onset of bipolar disorder; thus, the opportunity for prevention and/or early intervention exists. Evidence supports an association between mood disorders and weight gain. Psychotropic agents to treat bipolar disorder, particularly some second-generation antipsychotics, may be associated with weight gain. Obesity is associated with worse outcomes in bipolar disorder, so prevention of weight gain is clinically important. Environmental factors may contribute to relapse, so interventions to optimize social support systems are being evaluated. Pediatric bipolar disorder requires comprehensive management to achieve optimal outcome. Further research to study modifiable factors that contribute to its morbidity and chronicity is needed.

Introduction

Bipolar disorder represents a significant public health problem in children and adolescents. Preliminary evidence suggests that pediatric bipolar disorder is associated with a chronic treatment-resistant course [1]. Risk factors for treatment resistance must be identified to achieve optimal outcomes. Increased awareness of potentially modifiable psychiatric, medical, and psychosocial risk factors impacting on pediatric bipolar disorder may provide opportunities for prevention, early recognition, and timely intervention to improve prognosis.

This paper will first discuss the epidemiology of pediatric bipolar disorder. It then will review the impact of substance-related disorders, weight status, and social support systems on treatment. Interventions under study that may help optimize pediatric bipolar outcomes also will be presented.

Epidemiology

Many adults date the onset of their bipolar illness to childhood or adolescence. In a national survey, 31% of 500 adults with bipolar disorder reported their first mood symptoms appeared before age 14 years [2]. The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), a multicenter, prospective, naturalistic study of bipolar disorder funded by the National Institute of Mental Health, reported baseline data on its first 1000 subjects [3]. Participants were aged 15 years or greater. A total of 272 subjects (28%) reported that their first mood episode occurred before age 13 years (very early onset), 370 (37%) reported onset between ages 13 and 18 years (early onset), and 341 (35%) reported onset after age 18 years (adult onset).

The core clinical picture of bipolar disorder in childhood and early adolescence is still being defined [4••]. Although some children present with the classic mania symptoms of elation and grandiosity, many present with a predominantly irritable mood. Some children have discrete mood episodes, but others suffer mood disturbances so frequently that their illness has a nonepisodic or chronic quality. The lack of a clear-cut case definition has made it difficult to ascertain prevalence rates for very early-onset bipolar disorder in the general population [4••].

Bipolar disorder in mid to late adolescence has a presentation similar to that of adult-onset bipolar disorder [4••]. Lewinsohn et al. [5] examined bipolar prevalence rates in a community sample of 1709 adolescents aged 14 to 18 years. Bipolar disorder, mostly type II and cyclothymia, was identified in 18 adolescents (1% prevalence rate). The mean age of onset of the first affective episode in these subjects was 11.75 years. An additional 97 subjects (5.7%), designated the core positive group, did not meet full diagnostic criteria for bipolar disorder. However, they reported at least one persistent episode of

an abnormally elevated, expansive, or irritable mood. In adults, when the bipolar diagnostic spectrum is broadly defined and includes all subtypes, such as hypomania and cyclothymia, the prevalence has been reported as high as 9% [6].

Birth cohort studies suggest that the prevalence of affective disorders may be on the rise [7]. A cohort effect refers to a change in the rate of a disorder with each successive group of people born in the same decade or other designated time frame [8]. Gershon et al. [7] examined the lifetime prevalence rates of bipolar, schizoaffective, and unipolar disorders in 823 relatives of bipolar and schizoaffective patients born over the course of 6 successive decades (six birth cohorts). For all relatives, the lifetime prevalence of bipolar disorder and schizoaffective disorder in the pre-1940 birth cohorts was 8.8%, and 16.3% in the post-1940 cohorts ($P < 0.01$).

The cumulative hazard, or probability of developing bipolar illness by a given age, for each successive cohort was determined. With the exception of the cohort born between 1930 and 1939, analysis of cumulative hazard suggested that the risk of developing bipolar illness by a given age was increased for each successive cohort. The highest hazard was for cohorts born after 1940.

Anticipation studies examine the age of onset and severity of disease in successive generations. Lange and McInnis [9] reviewed eight anticipation studies that examined age of onset and frequency of bipolar episodes in families with high genetic loading for the illness. Some studies suggested that the age of onset may be decreasing by 6 to 16 years in the offspring relative to the parental generation. The offspring generation also reported two to four times increased frequency of episodes compared with the parental generation.

Analysis of an insurance database covering the lives of more than 1.7 million children aged less than 18 years revealed a significant increase in hospitalizations for a diagnosis of bipolar disorder between 1995 and 2000 [10]. The proportion of child and adolescent inpatients with bipolar disorder nearly doubled, from 10.6% to 18.4%. It could not be determined if the increase was due to changes in diagnostic practices, admission policies, or true prevalence changes.

Bipolar disorder is a major cause of disability globally among individuals aged 15 to 44 years [11]. Preliminary evidence suggests that school functioning is frequently impaired in children [12,13]. In adulthood, functional impairment affects employment and long-term interpersonal relationships and may lead to shortened life expectancy [11]. A self-report instrument that measured well-being and functioning across six domains was administered to 68 outpatients (age range 18 to 65 years) with bipolar disorder in remission [14]. Their mean scores were within or below the range of patients with eight chronic medical conditions, suggesting bipolar disorder has a major impact on quality of life.

Bipolar Disorder and Substance-related Disorders

Alcohol abuse/dependence

Relatively few studies have focused on substance-related disorders and their relationship to bipolar disorder in children and adolescents. In a 5-year naturalistic, prospective, follow-up study of 54 bipolar adolescents (mean age 16 years at entry), Strober et al. [15] found substance abuse in five (9%) subjects. However, sporadic substance abuse was documented in an additional 12 subjects (22%). In a recent meta-analysis of the phenomenology of pediatric bipolar disorder, seven studies including 362 bipolar youths over a span of 23 years were reviewed [16]. Only three of these studies reported the prevalence of substance use disorders, which ranged from 3.7% to 22.2%. West et al. [17] reported a 39% rate of substance abuse/dependence in 36 adolescent inpatients with bipolar disorder.

Alcohol use disorders can occur in childhood and early adolescence. Geller et al. [18] examined substance abuse patterns in a group of 25 adolescents with bipolar disorder (mean age of onset 9.6 years) and secondary substance dependency. First-time intoxication with alcohol occurred at a mean of 12.8 years, regular alcohol consumption at 14.0 years, and dependency at 15.3 years.

In a group of 72 adolescents referred to an inpatient substance abuse treatment program, Famularo et al. [19] reported six patients had the onset of alcohol abuse or dependence before age 13 years. Two thirds of the children had family histories of paternal alcoholism. Bipolar spectrum disorders were diagnosed in four of the six children. Three of the four children with bipolar illness had familial loading for bipolar disorder and a positive response to lithium.

Todd et al. [20] investigated the relationship between alcoholism and bipolar disorder in the relatives of 79 children with major depression followed prospectively for 5 years. Bipolar disorder was diagnosed in 25 children. Three of these children were adopted and not included in the study's analyses. Alcoholism (without an affective disorder) was reported in 20% of the 232 relatives of bipolar probands ($n = 22$), 12% of the 390 relatives of the depressed probands ($n = 54$), and 6% of the 313 relatives of normal controls ($n = 31$). Because probands had not fully gone through the age of risk for alcohol use disorders, familial transmission was analyzed in grandparents and parents. An affective disorder in either grandparent was associated with an increased risk for an affective disorder in the parent. Likewise, alcoholism in either grandparent was associated with an increased risk for alcoholism in the parent. However, alcoholism in grandfathers, but not grandmothers, was associated with an increased risk for a parental affective disorder (partial odds ratio [OR] = 3.93, 95% CI = 1.51–10.2). The authors recommended that there be heightened awareness for alcohol use disorders in the families of children with affective disorders.

Strakowski et al. [21] recently investigated the temporal relationship between bipolar disorder and alcohol use in 144 bipolar patients aged 12 to 45 years recruited from consecutive first-time psychiatric hospitalizations. Those with prior psychiatric hospitalizations were excluded to control for the confounding effects of chronicity. A total of 42% of the bipolar patients had a history of alcohol use disorders. A total of 33 of the 60 bipolar patients (55%) with alcohol use disorders had their bipolar disorder present first (Bipolar First), and 27 of the 60 patients (45%) had their alcohol use disorder present first (Alcohol First). Patients were followed for a mean of 2.6 years.

The Bipolar First group was significantly younger at the onset of bipolar illness (mean age 17 years) than the Alcohol First group (mean age 26 years). The age of onset of alcohol use was 19 years for the Bipolar First group and 18 years for the Alcohol First group. The Bipolar First group experienced a more severe illness course than either the Alcohol First group or the Bipolar Only group. Its members spent a significantly greater percentage of follow-up time in a full affective episode, usually mixed type. The Bipolar First group also spent a greater percentage of follow-up time with symptoms of an alcohol use disorder after discharge than the Alcohol First group. A total of 16 patients in the Bipolar First group developed their new-onset alcohol use disorder after their first hospitalization. Ten (62.5%) of these new-onset alcohol use disorders occurred in the first year after hospitalization.

Wilens et al. [22] investigated the risk of substance use disorders in adolescents with bipolar disorder. They compared 57 children who met lifetime *DSM IV* [23] criteria for bipolar disorder (mean age 13.3 years) with 46 control subjects (mean age 13.6 years) with no history of mood disorders. A substance use disorder was defined as any alcohol or drug abuse including dependence. Nicotine dependence was excluded. There was a significantly higher risk of substance use disorders in bipolar probands (n = 18, 32%) compared with controls (7%). This significant association was maintained even after adjusting for the effects of a comorbid conduct disorder. Substance use disorders followed the onset of bipolar disorder in the majority of cases (n = 15, 83%). A substance abuse disorder occurred within a year of the onset of bipolar disorder in six subjects and simultaneously in two subjects.

Geller et al. [18] conducted a randomized, double-blind, placebo-controlled clinical trial of lithium in 25 bipolar adolescents with secondary substance dependency. Lithium was superior to placebo as measured by significant improvement on ratings of global psychosocial functioning and significantly fewer positive drug assays. Optimal treatment of substance abuse in bipolar youth involves integration of multiple treatment modalities [24••].

Nicotine abuse/dependence

Cigarette smoking and exposure to tobacco smoke resulted in nearly 438,000 premature deaths in the United States during the period of 1997 to 2001 [25]. Among adults, deaths were due to cancer (39.8%), cardiovascular disease (34.7%), and respiratory disorders (25.5%). Although nicotine-dependent individuals with psychiatric illness comprise 7.1% of the US population, they consume more than one third of all cigarettes smoked [26]. Smoking rates in bipolar patients, based on small clinical samples, have ranged from 43% to 82% [27].

Despite the high prevalence of smoking, few studies have examined the clinical correlates of smoking and bipolar disorder. Waxmonsky et al. [27] examined the relationship between smoking and bipolar disorder in 1904 patients who were enrolled in the STEP-BD project. A total of 594 (31.2%) of these bipolar patients were current smokers, and 154 of the 594 (8.1%) smokers reported that they smoked more than one pack per day. Smoking was significantly associated with rapid cycling; suicide attempts; more severe depressive symptoms; greater psychosocial impairment; and higher rates of substance use (alcohol and illicit drugs), anxiety, psychosis, and attention-deficit hyperactivity disorder (ADHD).

Wilens et al. [28] compared cigarette smoking rates in a group of 31 bipolar adolescents relative to a comparison group of nonbipolar subjects with and without ADHD. There was a significantly higher rate of smoking in the bipolar probands (35%) than in the comparison group (12%). Cigarette smoking was significantly more likely to be associated with adolescent-onset bipolar disorder (age $\geq$ 12 years, 80%) compared with childhood-onset bipolar disorder (age $\leq$ 12 years, 14%). Bipolar disorder preceded the onset of cigarette smoking in 64% of the bipolar probands. Onset of smoking was earlier in the bipolar probands compared with controls (age 16.3 years vs 17.2 years). The authors suggested that prevention and early identification of smoking have relevance, as the behavior may lead to the use of other substances.

Bipolar Disorder and Weight Status

Another major public health problem is the rising rate of overweight status in children and adolescents. Overweight status is defined as gender-specific body mass index (BMI) for age at or above the 95th percentile on growth charts [29]. BMI is defined as weight in kilograms divided by height in meters squared [29]. The prevalence of overweight status in children and adolescents between the ages of 6 and 19 years tripled between 1980 and 2002 [29]. The National Health and Nutrition Examination Study [29] recently reported statistics on the overweight prevalence in a nationally representative sample of 3958 children and adolescents for 2003-2004. The prevalence of overweight status in this demographic group increased significantly, from 13.9% in 1999-2000 to 17.1% in 2003-2004.

The relationship between psychiatric disorders and obesity has been a topic of scientific interest but remains

seriously understudied, particularly in children and adolescents. Simon et al. [30] recently investigated the relationship between obesity and psychiatric disorders in a nationally representative sample of 9125 survey respondents (mean age 44.8 years). Participants were screened for psychiatric disorders with structured diagnostic interviews conducted by trained nonclinician interviewers. Lifetime prevalence rates of mood and anxiety disorders were significantly higher in obese individuals (BMI ≥ 30) compared with individuals who were not obese (BMI < 30). The positive association between mood disorders and obesity, as measured by ORs, was 1.21 (95% CI = 1.09–1.35) for major depression and 1.47 (95% CI = 1.12–1.93) for bipolar disorder. Although not able to conclude a causal relationship, the authors reported that almost 25% of obesity in the general population is attributable to an association with a mood disorder.

Studies of adults with bipolar disorder have reported higher prevalence of overweight status and obesity in bipolar subjects compared with age- and gender-matched community control subjects or reference normative values. Elmslie et al. [31] compared 89 euthymic bipolar outpatients from New Zealand with 445 community controls. Female bipolar subjects were significantly more likely to be overweight (44% vs 25%) or obese (20% vs 13%) or to have central adiposity (59% vs 17%) compared with reference subjects. Male bipolar patients were more likely to be obese (19% vs 10%) and significantly more likely to have central adiposity (58% vs 35%) compared with reference subjects. Overweight status was not significantly different between male patients and the reference group (29% vs 43%). Patients taking antipsychotic medications were significantly more likely to be obese than patients not treated with these medications.

McElroy et al. [32] assessed the prevalence of overweight status and obesity in an international sample of 644 adult patients (mean age 41.2 years) with *DSM IV* [23] bipolar disorder enrolled in the Stanley Foundation Bipolar Treatment Outcomes Network. Overall, 31% of the patients were overweight, 21% were obese, and 5% were extremely obese. American bipolar subjects (n = 478) had significantly higher BMIs and significantly higher rates of obesity and extreme obesity (BMI ≥ 40) compared with European bipolar subjects. The BMIs of the American subjects were compared with American reference values obtained from the National Health and Nutrition Examination Survey III [33] conducted between 1988 and 1994. Female bipolar patients had higher rates of obesity (23.6%) and extreme obesity (8.9%) but not overweight status (20%) relative to reference national norms (17.8%, 1.8%, 39%, respectively). Male bipolar patients had higher rates of overweight status (44.4%) and obesity (27.3%) but not extreme obesity (3.5%) compared with respective national norms (25.7%, 21.1%, 3.8%, respectively).

Longitudinal data on pediatric bipolar disorder and BMI in later adulthood do not exist. However, a small number of longitudinal, prospective studies have assessed the temporal relationship between childhood depression and subsequent weight status in adulthood. These studies may have relevance, as evidence suggests that nearly 50% of depressed children later develop a bipolar spectrum disorder [34].

Pine et al. [35] compared the BMIs of 90 children aged 6 to 17 years diagnosed with major depression with the BMIs of 87 age- and gender-matched control subjects. There was no significant BMI difference at baseline. Their BMIs then were compared 10 to 15 years after this initial assessment. At follow-up, subjects with a history of childhood major depression had a significantly higher mean BMI (26.1 ± 5.2) than subjects without a history of childhood depression (24.2 ± 4.1). BMIs did not differ between subjects who were (n = 11) and who were not (n = 166) depressed as adults at follow-up. Duration of depression from childhood into adulthood also was significantly associated with higher adult BMI.

Hasler et al. [36] conducted a community-based cohort study of 591 young adults (299 females, 292 males) to determine whether childhood depressive symptoms predicted problems with weight gain and obesity in adulthood. Subjects were aged 19 years at study entry. They were interviewed on five subsequent occasions. A total of 62% of the sample participated for 20 years. For women, childhood depressive symptoms before age 17 years were associated with greater increments in weight gain every 10 years compared with women without childhood depressive symptoms (4.8% vs 2.6% BMI increase per 10 years, $P < 0.05$). Women with childhood depressive symptoms were at significantly higher risk for obesity in adulthood (hazard ratio = 11.52, $P < 0.05$). In men, childhood depressive symptoms were associated with weight gain (not significant) but not obesity.

A recent prospective cohort study [37] investigated the weight status changes of 820 children and adolescents aged 9 to 18 years (403 females, 417 males) across a 20-year time span. Depression and anxiety disorders were assessed with structured diagnostic interviews at four different time points. BMI z scores (BMIz), which corresponded to growth chart percentiles, measured weight changes from childhood through adolescence. Females with a history of an anxiety disorder had a mean BMIz 0.13 units higher than females without a history of anxiety disorder, and this difference was maintained over time. Females with depression had greater yearly BMIz gains (0.09 units per year) than females without depression. Depending on height, these BMIz unit changes could correspond to weight differences of several kilograms. Anxiety and depressive disorders in males had no significant associations with weight status in adulthood.

Fagiolini et al. [38] longitudinally evaluated the impact of obesity on the clinical outcome of adult patients with bipolar disorder. A total of 62 of 175 (35.4%) patients with a *DSM IV* diagnosis of bipolar disorder met criteria

Table 1. Pharmacotherapy studies of pediatric bipolar disorder that report mean weight change

Reference	Design/duration, *months*	*N*	Mean age, *years*	Medication	Concomitant medications	Weight change*
Biederman et al. [41]	Open trial/1.9	30	10.1	Risperidone	Stimulants, other	+ 2.1 ± 2.0
DelBello et al. [42]	RCT/1.4	15	14.1	Divalproex + quetiapine	Other	+ 4.2 ± 3.2
Findling et al. [43]	Open trial/2.6	90	10.9	Lithium + divalproex	Stimulants, SGA, other	+ 3.0†
Frazier et al. [44]	Open trial/1.9	23	10.3	Olanzapine	Stimulants, other	+ 5.0 ± 2.3
Masi et al. [45]	Chart review/6.0	10	14.8	Clozapine	MSA	+ 7.0 ± 3.0
Pavuluri et al. [46]	Algorithm-based study/18.0	64	11.7	MSA alone, MSA + SGA, or SGA alone	Stimulants, other	+ 2.7†
Pavuluri et al. [47]	Open trial/6.0	37	12.1	Risperidone + MSA	Stimulants, other	+ 6.4†
Pavuluri et al. [48]	Open trial/6.0	34	12.3	Divalproex	Stimulants, SGA, other	+ 5.6 ± 4.3

*Mean gain (+) or loss (–) ± standard deviation (SD) in kilograms.
†SD not available for this study.
MSA—mood-stabilizing agent (ie, lithium or divalproex); RCT—randomized controlled trial; SGA—second-generation antipsychotic.

for obesity. Compared with the nonobese group, the obese patients reported significantly more depressive episodes, more manic episodes, higher baseline Hamilton Depression Rating scores, and more weeks in acute treatment before stabilization. A total of 125 patients completed acute treatment and entered maintenance therapy. Recurrence rates were significantly higher in the obese group, and time to recurrence was significantly shorter in the obese group.

Mood-stabilizing agents and antipsychotic medications, particularly second-generation antipsychotics, have been associated with weight gain in adults [39,40••]. There are few long-term, controlled trials in children and adolescents to determine weight changes associated with the pharmacologic treatment of bipolar disorder. The treatment of bipolar disorder with psychotropic agents in children and adolescents is largely based on adult randomized clinical trials; short-term, open-label child/adolescent trials; retrospective chart reviews; and case reports [24••].

Two recent articles reviewed pharmacotherapy studies of bipolar disorder in children and adolescents [4••,24••]. Pavuluri et al. [4••] reviewed prospective studies, primarily open trials, conducted in children and adolescents with bipolar disorder. Kowatch et al. [24••] presented studies that their consensus panel reviewed to develop treatment algorithms for the acute phase of bipolar disorder. Studies obtained from these two articles were examined to determine if they documented weight changes associated with the treatment of bipolar disorder. Table 1 summarizes studies [41–48] that met the following criteria: 1) Subjects were children and adolescents with a diagnosis of bipolar disorder, 2) the sample size was at least 10 subjects, and 3) mean weight change was documented or could be calculated for subjects. Three additional studies were not included due to incomplete quantitative data that were necessary to determine mean weight changes [49–51]. Due to differences in study design, duration, sample size, and use of concomitant medications, it was not possible to determine risk attributable to specific agents. However, a trend toward weight gain was noted with most regimens that included second-generation antipsychotics.

A recent literature review of medical morbidities associated with bipolar disorder reported that mortality from cardiovascular disease and pulmonary embolism may be elevated in bipolar patients compared with the general population [52]. Preliminary evidence also suggests that the prevalence of type II diabetes may be increased in patients with bipolar disorder relative to national norms [52]. The American Diabetes Association, in collaboration with the American Psychiatric Association, recently convened an expert consensus panel to review the health risks associated with the use of atypical antipsychotics and to develop monitoring recommendations [40••]. Losing weight and maintaining weight loss are challenging [38]. Interventions to prevent or minimize weight gain may prevent medical problems and improve the prognosis of bipolar patients. Unfortunately, information on medical morbidities in bipolar children and adolescents is lacking.

Psychosocial Risk Factors

Recently there has been attention paid to psychosocial factors that may precipitate or perpetuate bipolar disorder. The impact of supportive and nonsupportive interpersonal relationships on the course of bipolar disorder in

children and adolescents has been understudied. Geller et al. [53] reported significantly more impairment in parent and peer interactions of bipolar children compared with an ADHD comparison group and community controls. They also reported low maternal warmth was associated with relapse at a 2-year follow-up [54].

A small number of prospective studies report that bipolar adults with low social support or patients from families characterized by high expressed emotion (high-EE) are at greater risk of relapse and have longer times to recovery [55]. High-EE refers to a family environment of criticism, hostility, and overinvolvement [56]. Miklowitz et al. [57] assessed the impact of two family environment measures, EE and affective style (AS, negative vs benign), on relapse in 23 bipolar inpatients aged 18 to 30 years (mean 21 years). Most patients had been ill less than 2 years. Patients were followed for 9 months after hospital discharge. The association between high-EE homes and relapse almost reached significance ($P = 0.058$), and the association between a negative AS and relapse was significant ($P = 0.03$). The risk of relapse over the course of 9 months for patients from high-EE homes was estimated to be five times greater than the risk for patients from low-EE homes.

Family-focused psychoeducation (FFT) was designed to increase knowledge of the symptoms and treatment of bipolar disorder, enhance communication and support among family members, and foster coping and problem-solving skills. FFT has shown promise in adults [55]. Fristad et al. [58] investigated the treatment efficacy of multifamily psychoeducation groups in children with major mood disorders, including bipolar disorder. In this preliminary randomized controlled trial, parents reported increased knowledge about mood symptoms, and children reported more support from parents and peers compared with a waitlist control group.

Pavuluri et al. [59] recently reported preliminary results for a psychosocial intervention for pediatric bipolar disorder that combines FFT and cognitive-behavioral therapy with elements of social rhythm therapy. Social rhythm therapy stabilizes daily routines (mealtimes, exercise, sleep) that may help to maintain circadian integrity [60]. The disruption of social rhythms has been associated with the onset of manic episodes [61]. At the completion of treatment, 34 participants demonstrated significant reduction in symptoms of ADHD, aggression, mania, psychosis, depression, and sleep disturbance compared with pretreatment symptom severity.

Conclusions

Bipolar disorder in children and adolescents is a major public health problem associated with significant functional impairment. Preliminary evidence suggests that children and adolescents with bipolar disorder may be at increased risk for substance-related disorders, weight problems, and impaired social support systems. Systematic studies are needed to determine the true prevalence of these problems that may contribute to treatment resistance.

Affective disorders and/or alcoholism in a parent may confer increased risk to offspring, so obtaining a detailed family history is important. Early evidence suggests alcohol use disorders often follow the onset of pediatric bipolar disorder. Comorbid alcohol use disorders are associated with a more complicated course of illness. Their prevention or early intervention may improve outcome in bipolar patients, but more systematic study is needed. Further investigation into the genetic and environmental aspects of familial alcoholism and affective disorders also appears warranted.

Youths with bipolar disorder also are at increased risk for nicotine dependence. In adults, smoking has been associated with several comorbid psychiatric disorders, including anxiety disorders, ADHD, and substance abuse. Although further research is needed, optimal treatment of these comorbid conditions in children and adolescents with bipolar disorder may improve psychiatric outcomes and help to prevent the onset of tobacco use. Quitting the smoking habit is challenging and often only successful after multiple attempts [62]. Given the high health costs of tobacco use, prevention is of paramount importance.

Preliminary research supports an association between mood disorders and weight gain. Prospective studies have demonstrated a relationship between childhood depression and increased weight status in adulthood. Obesity in adults with bipolar disorder has been associated with worse outcomes and medical complications. Psychotropic agents to treat bipolar disorder, particularly some second-generation antipsychotics, may be associated with weight gain, so weight monitoring should be incorporated into treatment plans.

Most studies on the psychosocial aspects of bipolar disorder have focused on adults and suggest that the lack of social support or family environments characterized by high-EE impacts negatively on the course of bipolar disorder. Initial evidence suggests that bipolar children and adolescents may have difficulties in relationships with family members and peers. Interventions to improve social support, coping skills, and communication and to stabilize daily routines are being evaluated.

In summary, pediatric bipolar disorder is difficult to treat and requires comprehensive management. Many preventable or potentially modifiable risk factors can complicate the treatment course. Further public health research is needed to determine if prevention and early intervention to address these treatment resistance factors can impact on the morbidity and chronicity of this illness.

Acknowledgments

None of the authors has a potential conflict of interest, financial or otherwise.

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