Bipolar Spectrum Disorder: Improving Its Recognition and Diagnosis

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The lifetime prevalence of bipolar I disorder is approximately 1%. However, the prevalence of bipolar spectrum disorder is substantially higher. Bipolar spectrum disorder is a longitudinal diagnosis characterized by abnormal mood swings comprising some of the following cross-sectional clinical states: mania, hypomania, mixed states, hyperthymic temperament, major depressive episode, and depressive mixed state. Most bipolar spectrum patients present for treatment during a depressive episode, and therefore clinicians often miss the diagnosis of bipolar spectrum disorder. Several studies have documented that patients often wait as long as 10 years for the correct diagnosis of bipolar spectrum disorder. One way to increase recognition of bipolar spectrum disorder is to screen for it. A recently introduced screening instrument for bipolar spectrum disorder, the Mood Disorder Questionnaire, is described.

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The prevalence of bipolar disorder is generally considered to be 1%, evenly divided between men and women.[1] In fact, this is the lifetime prevalence of bipolar I disorder. The prevalence of bipolar spectrum disorder is considerably higher. A recent review[2] of research on the prevalence of bipolar spectrum disorder reported on 9 studies worldwide. These studies were all population-based and utilized standardized, structured research diagnostic interviews. These studies reported a range of 2.6% for a 6-month prevalence to 7.8% for a lifetime prevalence of bipolar spectrum disorder, with a median of 3.4%. These studies did not use a standard definition for bipolar spectrum disorder, but in general included bipolar I and bipolar II disorders, and sometimes cyclothymia (Table 1).

Others have proposed more inclusive definitions of bipolar spectrum disorder. In 1992, Young and Klerman[4] proposed inclusion of 6 different clinical states, including those with unipolar depression in families heavily loaded with bipolar disorder (Table 2). More recently, Akiskal and Pinto[5] proposed a bipolar spectrum with 7 subtypes (Table 3), including masked bipolarity and hyperthymic depression.

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CROSS-SECTIONAL CLINICAL STATES

Bipolar spectrum disorder is a longitudinal diagnosis involving abnormal mood swings, including mania, hypomania, mixed states, hyperthymic temperament, major depressive episode, and depressive mixed state. Mania is a persistent elevation of mood with accompanying symptoms and severe psychosocial impairment.[3] Hypomania is similar to mania, but less severe. In mixed states, criteria for both mania and major depressive episodes (except for duration) are met for nearly every day during at least a 1-week period. Depressive mixed states are characterized by unrelenting dysphoria and irritability, extreme fatigue, racing thoughts, anxiety and panic attacks, and suicidal obsessions and impulses (Table 4).[6] Hyperthymic temperament includes attributes that constitute a part of the long-term functioning of the individual. Individuals with hyperthymic temperament are generally thought of as extremely outgoing and ambitious types (Table 5).[6,7] Such individuals are often quite successful in business and sales, although their grandiose and risk-taking attitudes may at times cause serious legal, financial, or interpersonal problems.

TREATMENT-SEEKING BEHAVIOR

Most patients with bipolar spectrum disorder seek treatment for depression, rather than mania or hypomania. In a recent survey of its members, the National Depressive and Manic-Depressive Association (DMDA) found that 60% of its members with bipolar spectrum disorder sought treatment because of depression (R. M. A. H., unpublished data, 2000). Other reasons included anxiety symptoms, difficulty sleeping, and substance abuse. Patients rarely present with

Table 1. Bipolar Spectrum Disorders as Defined by DSM-IV[a]

Disorder	Manic and Mixed Episodes	Hypomanic Episodes	Depressive Episodes
Bipolar I	✓	*	*
Bipolar II	...	✓	✓
Cyclothymia	...	*	Not major depressive disorder

[a]Based on DSM-IV.[3] Symbols: ✓ = must have, * = may have.

Table 2. Proposal of 6 Subtypes of Bipolar Spectrum Disorder[a]

Type	Characteristics
Bipolar I	Depression with full-blown mania
Bipolar II	Hypomania and depression
Bipolar III	Hypomania and depressive symptoms
Bipolar IV	Secondary to disease or drugs
Bipolar V	Major depression with a family history of bipolar disorder
Bipolar VI	Unipolar mania

[a]Based on Young and Klerman.[4]

Table 3. Proposal of 7 Subtypes of Bipolar Spectrum Disorder[a]

Type	Characteristics
Bipolar I	Depression with full-blown mania
Bipolar I½	Depression with protracted hypomania
Bipolar II	Depression with hypomania
Bipolar II½	Cyclothymic depression
Bipolar III	Antidepressant-associated hypomania
Bipolar III½	Bipolarity masked—and unmasked—by stimulant abuse
Bipolar IV	Hyperthymic depression

[a]Based on Akiskal and Pinto.[5]

Table 4. Clinical Picture of Depressive Mixed States[a]

Unrelenting dysphoria and irritability
Psychomotor agitation and restlessness
Extreme fatigue
Racing thoughts
Free-floating anxiety as well as panic attacks
Unendurable sexual excitement
Intractable insomnia
"Histrionic" appearance yet genuine expressions of depressive suffering
Suicidal obsessions and impulses

[a]Reprinted from Akiskal,[6] with permission.

Table 5. Attributes, Assets, and Liabilities of Hyperthymic Temperament[a]

Cheerful and exuberant
Articulate and jocular
Overoptimistic and carefree
Overconfident, self-assured, boastful, and grandiose
Extroverted and people-seeking
High energy level, full of plans
Versatile with broad interests
Overinvolved and meddlesome
Uninhibited and stimulus-seeking

[a]Adapted from Akiskal,[7] with permission.

hypomania and, when manic, come to attention because of intervention by family or legal authorities. Unfortunately, in their assessments of patients with depression, physicians often neglect to ask about a history of mood swings and mania. Consequently, the diagnosis of bipolar spectrum disorder is often missed. For example, in a study of 108 consecutive outpatients with depression or anxiety in a private family practice setting, 26% had the diagnosis of bipolar spectrum disorder, the majority of whom had bipolar II disorder.[8] In Italy, Perugi et al.[9] assessed 86 consecutive day-hospital patients and outpatients with DSM-IV major depressive episode with atypical features (i.e., mood reactivity, weight gain, hypersomnia, leaden paralysis, and rejection sensitivity). They found that 72% of these patients had bipolar spectrum disorder, over one half of whom had bipolar II disorder. This represented one third of the depressed group. In a recent study of patients seen in an outpatient clinic over the course of 1 year,[10] 37% experienced a manic or hypomanic episode, but were misdiagnosed as having unipolar depression.

MISSED AND DELAYED DIAGNOSIS

This lack of recognition of and attention to the possibility of bipolar spectrum disorder leads to substantial delay in patients' receiving an accurate diagnosis. In a survey of its members completed in the early 1990s,[11] the National DMDA found that nearly one quarter of patients consulted a professional within 6 months of onset of their symptoms. However, 48% consulted 3 or more professionals before receiving a correct diagnosis, and 10% consulted 7 or more professionals. Thirty-four percent waited 10 years or more for their first diagnosis of bipolar disorder. In another sample of bipolar patients entering the Stanley Foundation Bipolar Treatment Outcome Network,[12] the average length of time for first treatment of bipolar disorder was 10 years. In the most recent National DMDA survey, the results were nearly identical: 34% of National DMDA members reported waiting 10 years or more for their first accurate diagnosis of bipolar disorder (R. M. A. H., unpublished data, 2000).

This delay in diagnosis often has substantial adverse results. Patients do not get the appropriate treatment to alleviate their symptoms. They may even get treatments that exacerbate their symptoms, such as prescription of antidepressants precipitating mania and producing rapid cycling. They continue the unfortunate behaviors that are destructive to themselves and their loved ones.

CLINICAL COURSE

Patients with bipolar spectrum disorder in general have stable clinical courses in terms of diagnosis. In a 10-year follow-up of patients in the National Institute of Mental Health Collaborative Program on the Psychobiology of Depression,[13] two thirds (66%) of patients with bipolar I

disorder had a manic episode during the follow-up period, whereas only 7.5% of bipolar II patients had a manic episode during the follow-up period. Over one third (34%) of bipolar II patients had at least one hypomanic episode. Among those who had a diagnosis of nonbipolar depression at index, only 5% had a hypomanic episode and 5.2% had a manic episode during the 10-year follow-up.

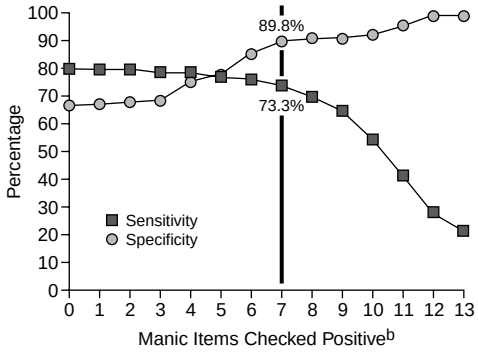
A substantial problem in the treatment of bipolar depression is the risk of switching (i.e., precipitating mania or hypomania). Data from a number of studies, particularly the work of Wehr and Goodwin,[14,15] suggest that monoamine oxidase inhibitors and tricyclic antidepressants, when used without concurrent mood stabilizers, are likely to induce switching in patients with bipolar spectrum disorder. Angst,[16] however, has argued that the increase in the rate of switching with the introduction of antidepressants is due not to a genuine increase in the switch rate, but to an increase in the number of patients admitted for treatment for affective disorders in recent years. Many clinicians also believe that the newer antidepressants, such as bupropion and the selective serotonin reuptake inhibitors, are less likely to induce switches than the tricyclic antidepressants and monoamine oxidase inhibitors.[17]

The most serious outcome of bipolar spectrum disorder is suicide. In their analysis of then-existing studies of suicide in bipolar patients, Goodwin and Jamison[18] reported a weighted mean suicide rate of 18.9%. Do people with bipolar spectrum disorder commit suicide during the depressed state, mixed state, or manic state? Isometsa et al.[19] identified 31 people with bipolar I disorder among 1397 people who committed suicide in Finland within a 12-month period. They found that 79% committed suicide during an episode of major depression, and only 11% during a mixed state and 11% during a psychotic manic state.

SCREEN FOR BIPOLAR SPECTRUM DISORDER

One method of increasing recognition of bipolar spectrum disorder is to screen for it. A brief and easy-to-use screening instrument for bipolar spectrum disorder, the Mood Disorder Questionnaire (MDQ), has recently been developed and tested.[20] The MDQ is a self-report, single-page, paper-and-pencil inventory that can be quickly and easily scored by a physician, nurse, or any trained medical staff assistant. The MDQ was designed by a committee comprising experts in bipolar disorder and instrument development and representatives of 2 major patient advocacy organizations. The MDQ screens for a lifetime history of a manic or hypomanic syndrome by asking 13 yes/no items derived from the DSM-IV criteria and from clinical experience (Appendix 1). An additional yes/no question asks whether several of any reported manic or hypomanic symptoms or behaviors were experienced concurrently. Finally, the level of functional impairment due to these symptoms is also assessed.

Figure 1. Operating Characteristics of the Mood Disorder Questionnaire as a Function of Number of Positive Mania Items[a]



[a]Reprinted from Hirschfeld et al.,[20] with permission. Thick vertical line designates the cutoff point for a positive screen.
[b]With at least some items occurring concurrently and causing moderate impairment.

The MDQ underwent 2 developmental stages. The first involved administering a draft version to patients with bipolar disorder to assess feasibility and face validity of the items. A revision was performed on the basis of this experience.

The MDQ was validated in a study conducted at 5 outpatient psychiatric clinics with special expertise in mood disorders.[20] After providing informed consent, patients filled out the MDQ. A random subsample of these patients received a research diagnostic interview (the Structured Clinical Interview for DSM-IV [SCID]) within 2 weeks by a trained interviewer to obtain a diagnosis of bipolar spectrum disorder (including bipolar I, bipolar II, and bipolar disorder not otherwise specified). The interviewer was blind to the clinical diagnosis of the patient and to the MDQ results. A group of 198 patients received the telephone diagnostic interview, of whom 63% were female, and the mean age was 44 years. Fifty-five percent of the patients received a research (SCID) diagnosis of bipolar spectrum disorder.

A data analysis was performed comparing the MDQ results and the research diagnosis. Sensitivity and specificity were calculated using the following procedure:

A positive screen would result if all 3 criteria were met:

1. The patient marked "Yes" for question 2 (co-occurrence);
2. The patient marked "Moderate" or "Serious" for question 3 (impairment); and
3. The patient marked "Yes" to N (a number from 1 to 13) of the symptoms in question 1.

Sensitivity and specificity were calculated for each value of N and were plotted (Figure 1). Sensitivity refers to the proportion of people with bipolar spectrum disorder who

have a positive screen. The higher the sensitivity, the better the MDQ correctly selects someone with bipolar spectrum disorder. Specificity is the mirror opposite, referring to the proportion of people who do not have bipolar spectrum disorder who have a negative screen. Specificity measures how well the MDQ correctly rules out someone who does not have bipolar spectrum disorder. This is important because the "cost" of incorrectly screening "in" someone who does not have bipolar spectrum disorder is high.

A cutoff point of a minimum of 7 was selected for a positive screen. This cutoff provided good sensitivity (0.73, 95% confidence interval [CI] = 0.65 to 0.81): 7 of 10 patients with bipolar disorder are correctly identified. It also provided very good specificity (0.90, 95% CI = 0.84 to 0.96): 9 of 10 people who do not have bipolar disorder are accurately screened out. Threshold cutoffs higher than 7 resulted in a loss of sensitivity without a considerable increase in specificity, while lower cutoffs resulted in a loss of specificity. These characteristics are quite consistent with screening instruments for psychiatric illnesses.

The MDQ can be filled out in doctors' offices. It can also be accessed on the Web site of the National DMDA (www.ndmda.org). In addition, it will be accessible by the Web sites of other organizations, as well as Web sites of several manufacturers of medications used to treat bipolar disorder.

The MDQ can help family members and other interested people to identify patients suffering from bipolar disorder and to encourage them to get help. Hopefully these kinds of efforts, along with educational programs aimed at raising the consciousness about bipolar disorder among health care professionals and among the general public, will serve to increase recognition, improve treatment, and ensure appropriate and timely treatment for those who suffer from bipolar disorder.

CONCLUSIONS

Prompt diagnosis and treatment of bipolar spectrum disorder can literally save lives. Bipolar spectrum disorder is still an evolving concept, and many clinicians remain unaware of how prevalent bipolar spectrum disorder may be in their practice. As the classic notion of bipolar I, comprising episodes of depression and full-blown mania, gives way to a new bipolar spectrum concept of various clinical states, many patients will correctly be identified and treated.

Because bipolar patients are much more likely to seek treatment for their depressive states than for their manic or hypomanic states, clinicians should consider the possibility of bipolar spectrum disorder for all patients presenting for treatment of major depression. Although the clinical presentation of bipolar and unipolar depression are virtually identical, a history of mania or hypomania must be taken into consideration by the clinician when initializing a treatment plan. Treating a bipolar patient as a unipolar depressed patient may be a recipe for making a bad situation worse. Antidepressant treatment in bipolar spectrum disorder patients may only exacerbate the problem by inducing switching or rapid cycling.

Untreated mania can lead to major psychosocial, legal, or financial problems for patients. Yet most patients will not seek medical help when they are in such states. Thus, it is all the more crucial that bipolar spectrum disorder be recognized when the patient seeks medical help for depression or other problems. It is unfortunate that most clinicians still neglect to ask the right questions of their patients to make a bipolar spectrum disorder diagnosis.

The Mood Disorder Questionnaire was designed to address these problems. Screening depressed or anxious patients for bipolar spectrum disorder before initializing a treatment plan may be the best way to increase the recognition of bipolar spectrum disorder and decrease misdiagnosis. Because the MDQ is easy to administer and score, the cost of screening is nominal. By contrast, the cost of misdiagnosis is high—high for the untreated patient, high for the patient's family or loved ones, and, ultimately, high for society as a whole. The sensitivity and specificity of the MDQ in detecting bipolar spectrum disorder are quite good, and the instrument could provide an effective screen in clinical settings. But perhaps most importantly, the MDQ could have an even more pervasive impact by raising the level of awareness of bipolar spectrum disorder among clinicians and fostering a greater understanding of this pernicious spectrum of disorders that create havoc in the lives of so many.

Drug name: bupropion (Wellbutrin).

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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Appendix 1. The Mood Disorder Questionnaire[a]

1. Has there ever been a period of time when you were not your usual self and…	Yes	No
… you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?	❑	❑
… you were so irritable that you shouted at people or started fights or arguments?	❑	❑
… you felt much more self-confident than usual?	❑	❑
… you got much less sleep than usual and found you didn't really miss it?	❑	❑
… you were much more talkative or spoke much faster than usual?	❑	❑
… thoughts raced through your head or you couldn't slow your mind down?	❑	❑
… you were so easily distracted by things around you that you had trouble concentrating or staying on track?	❑	❑
… you had much more energy than usual?	❑	❑
… you were much more active or did many more things than usual?	❑	❑
… you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?	❑	❑
… you were much more interested in sex than usual?	❑	❑
… you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?	❑	❑
… spending money got you or your family into trouble?	❑	❑

2. If you checked "Yes" to more than one of the above, have several of these ever happened during the same period of time? *Please circle one response only.*

Yes No

3. How much of a problem did any of these cause you—like being unable to work; having family, money, or legal troubles; getting into arguments or fights? *Please circle one response only.*

No problem Minor problem Moderate problem Serious problem

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