

## Bipolar disorder: diagnostic issues

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The term bipolar disorder applies to a range of conditions that are likely to have different aetiologies, including genetic or family vulnerability, precipitation by stressful life events, physical illness or drugs including antidepressants. The essential features of bipolar disorders are cyclical mood disorders including distinct sustained periods of mood elevation. Mood elevation is critical in differentiation from unipolar disorders, specifically major depressive disorder, recurrent type.

Bipolar disorders are classified in a number of ways. One diagnostic system is described in the *Diagnostic and statistical manual of mental disorders*, fourth edition, text revision (DSM-IV-TR),<sup>1</sup> which is United States based; another is described in the *International statistical classification of diseases and related health problems*, 10th revision (ICD-10),<sup>2</sup> which is World Health Organization and predominantly European based. Although these diagnostic classifications have similarities, there are several differences in their detail. Here we refer to the DSM-IV-TR<sup>1</sup> criteria, unless otherwise specified. Box 1 provides a summarised approach to classifying bipolar disorder.

### Types of bipolar disorder

Bipolar disorder is divided into a number of types and subtypes, depending on the patient's history, the clinical presentation phase (elevated, depressed, rapid cycling or otherwise), the duration and severity of symptoms, and associated features. These factors are important as they help to indicate the likely outcome of current and future illness episodes, and inform possible treatments.

### Bipolar I disorder

#### Mania

The most florid presentation of bipolar disorder is type I, in which mood elevations are marked and include clinical features of mania (see Box 2 for a guide derived from DSM-IV-TR criteria for a manic episode<sup>1</sup>). This illness has a distinct period of abnormality with persistently elevated, expansive, or irritable mood lasting at least a week, or requiring hospitalisation.

Individuals who are manic will experience disturbances in their perception, thinking and behaviour, which are largely determined by their illness rather than by external circumstances. For instance, while a patient is psychotic, he or she may report hallucinations such as voices saying he or she is wonderful and the leader of the people, or even a representative of God. These hallucinations are usually, but not always, consistent and congruent with patients' mood states. They may have grandiose thinking patterns, incongruent with their actual circumstances in life. They may, for example, believe they are extremely powerful, king of the world, or even "the Messiah".

Thinking can be so fast that the patient's speech cannot keep up. Patients may be distractible, expansive and irritable. Although at first they might seem able to multitask, they usually end up moving from one activity to another in a distracted fashion. As the illness worsens, they tend to become more disorganised.

Typically, the need for sleep is reduced; patients may feel rested after only 2 or 3 hours of sleep, and may be so preoccupied and

### ABSTRACT

- Bipolar disorders are cyclical mood disorders with clinical features including distinct sustained periods of mood elevation.
- Briefer (4 days or more), mild episodes of mood elevation define bipolar II disorder; lengthier (7 days or more), more severe episodes (or those requiring hospitalisation), with or without psychotic features, define bipolar I disorder.
- Depressive periods are more common and lengthier than manic or hypomanic states, and are the main cause of disability.
- Bipolar depression may respond poorly to antidepressants and these medications may destabilise the illness. The diagnosis of bipolar disorder should be considered when a patient with depression is treatment resistant.
- Irritability is a common symptom in bipolar disorder, particularly during mixed states (during which patients have features of mood elevation and depression concurrently) or when there is rapid cycling of mood (more than four episodes of mood disorder per year).
- Alcohol misuse and use of illicit drugs may simulate mood changes in bipolar disorder.
- Accurate diagnosis and assessment of bipolar disorder is essential for clinical decision making and determining prognosis and treatments.

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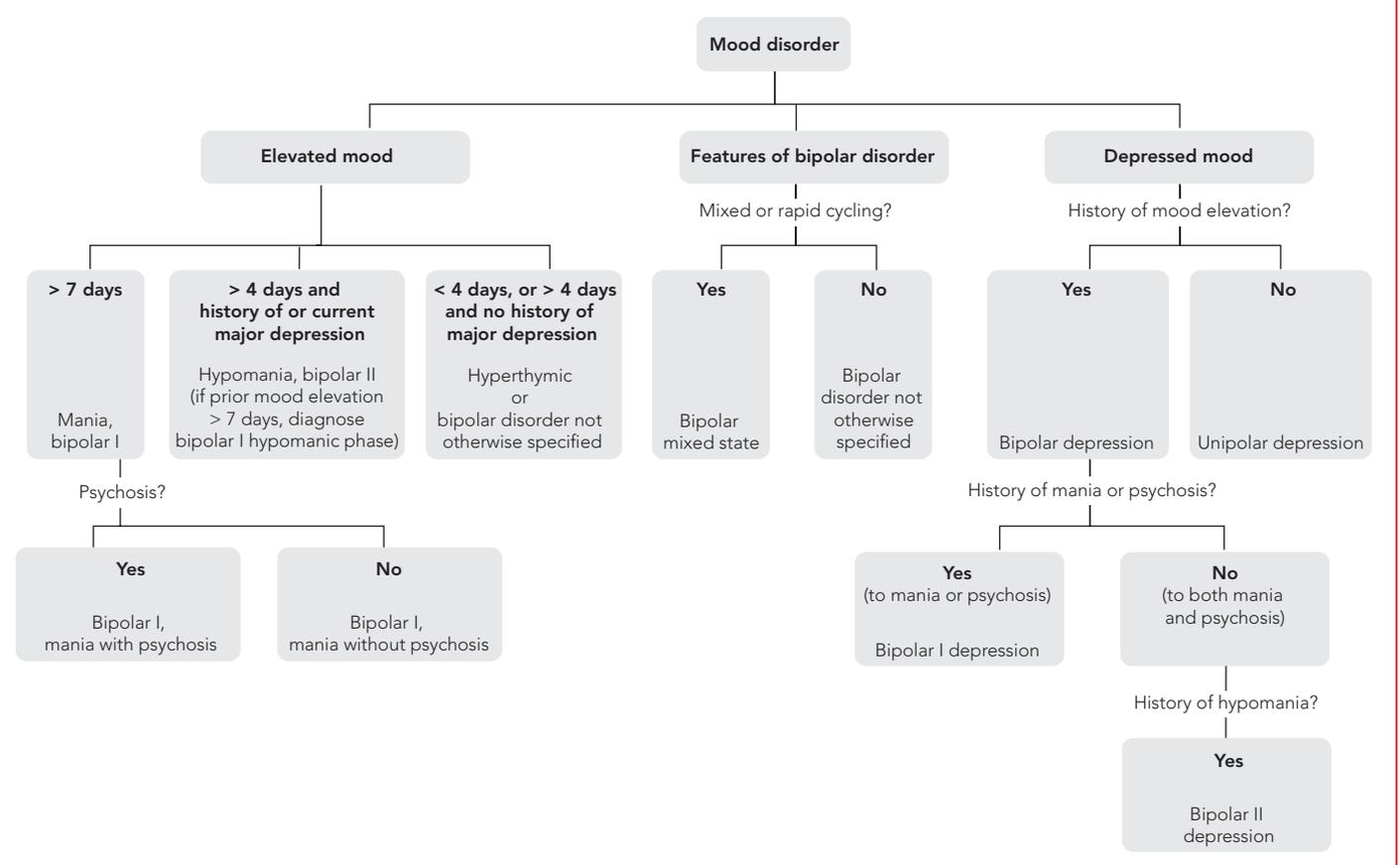
active that they do not consume enough food and fluids. If this persists, they may collapse from exhaustion. They tend to be socially disinhibited, loud and intrusive, and have impaired judgement. Risk taking can increase — for example, driving too fast, drinking excessive amounts of alcohol or using illicit drugs. Patients may gamble exuberantly or spend excessively, beyond their normal budget and financial resources. Sexual arousal and libido may increase during mania and patients can get into sexual misadventures with partners who they may never have chosen when not ill. This may lead to unprotected sex and expose patients to sexually transmitted diseases. These complications can add to the burden of disease and disability, including financial complications such as bankruptcy.

Although patients with bipolar disorder can seriously endanger their lives by these high-risk activities, including activities undertaken while under the influence of drugs or alcohol, they rarely attempt or commit suicide during this phase of the illness. Nonetheless, they are at increased risk of accidents and may die by misadventure.

### Depression

Although bipolar disorder is defined by mood elevation, the greatest disability and risk occurs during depression, which is typically the dominant phase of the illness, especially for those who are untreated. Depression typically takes up 30%–50% of the

1 Diagnosis of bipolar disorder



patient's life and mania takes up about 5%–10%, with a semblance of normality making up the remainder of the patient's life.<sup>3-5</sup>

It is common for individuals to have one or more episodes of bipolar depression before their first manic episode. An initial diagnosis of major depressive disorder is often made until a manic episode results in a change of diagnosis to bipolar I disorder.

Features of depression associated with bipolar disorder (referred to as bipolar depression) are essentially the same as those of major depression (see Box 3 for a guide derived from DSM-IV-TR criteria for a major depressive episode<sup>1</sup>) but occur in patients with a history of mania or hypomania. Depressive features themselves cannot distinguish bipolar disorder from unipolar depression, although some features appear more commonly in bipolar disorder.<sup>6</sup> These include the tendency to have atypical features of depression, with symptoms such as hypersomnia (rather than insomnia) and hyperphagia (rather than anorexia). These features are indicative, rather than diagnostic, of bipolar depression. The presence of psychotic symptoms in the depressive phase also suggests an increased likelihood of bipolar disorder (see Mitchell et al, page S10).<sup>7</sup>

During bipolar depression, patients can feel desperate about the depth and severity of and disability from their low mood. They may not recall or be able to think of the prospect of returning to normal mood and normal life — they may not even recall antecedent mood elevations. They can also feel suicidal; 10%–19% of patients diagnosed with bipolar disorder commit suicide.<sup>8</sup>

Suicide usually occurs during a depressive episode (79%)<sup>9</sup> when the risk of suicide is 15 times that of the general population.<sup>10</sup> Patients with bipolar disorder who have attempted suicide are over four times more likely than those who have not attempted suicide to subsequently attempt or complete suicide.<sup>11</sup>

As bipolar depression requires different treatments than those used for unipolar depression, treatment resistance (ie, the loss of effectiveness of antidepressants that initially appeared effective) may be a hint of bipolar disorder. Although this may seem paradoxical, antidepressants may be ineffective, only briefly effective or more destabilising than helpful for many patients with bipolar disorder. Antidepressant use is more likely to increase the rate of mood cycling, induce mood elevation or result in a mixed state than mood-stabilising agents (see Malhi et al, page S24).<sup>12</sup>

**Bipolar II disorder**

**Hypomania**

Bipolar II disorder is characterised by cyclical mood and defined by mood elevation in a patient who has had at least one or more major depressive episodes. The persistently elevated, expansive or irritable mood (referred to as hypomania) only needs to last at least 4 days (see Box 4 for a guide derived from DSM-IV-TR criteria for a hypomanic episode<sup>1</sup>), rather than a week as in mania; however, if the patient is hospitalised during hypomania, the diagnosis becomes bipolar I disorder. The ICD-10<sup>2</sup> criteria

**2 Guide for diagnosing a manic episode\***

- A. A distinct period of abnormally and persistently elevated, expansive or irritable mood, lasting at least 1 week.
- B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and are significant:
- (1) inflated self-esteem or grandiosity
  - (2) decreased need for sleep
  - (3) more talkative than usual
  - (4) flight of ideas or feeling that thoughts are racing
  - (5) distractibility
  - (6) increase in goal-directed activity, or agitation
  - (7) excessive involvement in pleasurable but high-risk activities (eg, buying sprees, sexual indiscretions or foolish investments).
- C. The symptoms do not meet criteria for a mixed episode.
- D. The mood disturbance is sufficiently severe to cause marked impairment in functioning or in usual social activities or relationships with others, or there are psychotic features.
- E. The symptoms are not due to the direct physiological effects of a drug of misuse or medication, or a general medical condition (eg, hyperthyroidism).

\* Derived from the *Diagnostic and statistical manual of mental disorders*, fourth edition, text revision.<sup>1</sup> ◆

differentiate hypomania on the basis of a persistent mild elevation of mood with less disorganisation than in mania, rather than the more marked mood elevation and disorganisation of mania.

Patients may experience elevation in quite a subtle way that they perceive as constructive and refer to as “my usual self”. In this phase, they may need less sleep than normal yet do not feel tired. They may feel more creative than usual, active, alive, energetic and productive, and can indeed be so. Sociability and sex drive increase, and risk taking may occur. Patients can present as the “life and soul of a party”. Patients are unlikely to present to doctors with hypomania. They may value hypomania as their preferred state, and they can feel that a normal mood is “below par” or describe normal mood as “depressed”. Although some patients may make disadvantageous business and personal decisions because their judgement is affected by their illness, others can be extraordinarily successful through taking business or personal risks. The diagnosis of hypomania is typically made in retrospect and it is helpful to interview a significant other when making the diagnosis; comments such as “he is up and down like a yoyo” may reflect hypomania.

**Depression**

Bipolar II depression is like unipolar depression and bipolar I depression. The history of hypomania allows a bipolar II disorder diagnosis. Frequent relapses and/or development of resistance to antidepressant treatments should alert the clinician to the possibility of bipolar II disorder.

Although it might seem that bipolar II disorder is a less severe illness than bipolar I disorder, it can be associated with increased disability. Although elevated mood is less severe, patients spend more time in the depressive phase of their illness,<sup>3</sup> and may be severely ill and suicidal. As with bipolar I disorder, the dominant phase of this illness is depression.

**Mixed episodes**

Mixed episodes occur when patients have features of mood elevation and depression simultaneously. DSM-IV-TR<sup>1</sup> criteria for a mixed episode require that the patient has full features of both mania and depression. Using this approach, mixed episodes do not include mixed states where only some criteria are met, or states in which there are simultaneous features of both elevation and depression but not the severity of either mania or major depression. Many experts in psychiatry view the DSM-IV-TR<sup>1</sup> criteria as being too strict and limiting. In contrast, ICD-10<sup>2</sup> criteria allow for the diagnosis of a mixed episode in the presence of either of a mixture of manic and depressive symptoms or a rapid alteration between manic and depressive symptoms.

Clinicians must be mindful that mania and depression can coexist, and that patients with bipolar disorder may present as angry, irritable and dysphoric. In these circumstances, antidepressants may worsen symptoms.

**Bipolar disorder not otherwise specified, and bipolar spectrum**

When there is no clear category for a patient’s diagnosis, yet they have had features of mood elevation and depression, with disability, the term bipolar disorder not otherwise specified can be used. Some experts have broadened the diagnosis of bipolar disorder to include a range of disorders and disabilities with a central quality of cyclical mood disorder, yet not strictly meeting criteria for bipolar I, bipolar II or a mixed state.

Some experts argue strongly that the traditional definition of bipolar disorder is too narrow and that milder indicators of mood elevation should be viewed as part of the bipolar spectrum. For instance, if a patient’s mood becomes elevated during treatment with an antidepressant, during a medical illness or while under the

**3 Guide for diagnosing a major depressive episode\***

- A. Five (or more) of the following symptoms have been present during the same 2-week period and at least one is either (1) depressed mood or (2) loss of interest or pleasure:
- (1) depressed mood most of the day, nearly every day
  - (2) marked loss of interest or pleasure in all, or almost all, activities
  - (3) significant weight loss when not dieting, or weight gain, or altered appetite
  - (4) insomnia or hypersomnia nearly every day
  - (5) psychomotor agitation or retardation nearly every day
  - (6) fatigue or loss of energy
  - (7) feelings of worthlessness or excessive or inappropriate guilt
  - (8) loss of ability to think or concentrate, or indecisiveness
  - (9) recurrent thoughts of death, suicidal ideation without a plan, a suicide attempt, or a specific plan for committing suicide.
- B. The symptoms do not meet criteria for a mixed episode.
- C. The symptoms cause clinically significant distress or impairment.
- D. The symptoms are not due to the direct physiological effects of a drug of misuse or medication, or a general medical condition (eg, hypothyroidism).
- E. The symptoms are not better accounted for by bereavement.

\* Derived from the *Diagnostic and statistical manual of mental disorders*, fourth edition, text revision.<sup>1</sup> ◆

influence of illicit drugs, they could be classified under the category of bipolar disorder. Individuals with certain personality types — such as those who are mostly ebullient, buoyant and especially optimistic, or those who are emotionally over-reactive and may be diagnosed with borderline personality disorder — show evidence of so-called soft bipolarity. It has been proposed that such patients should be referred to as having bipolar disorder. These ideas are controversial, and the roles of traditional mood stabilisers have not been established in these states.

### Anxiety and bipolar disorder

Although mania or hypomania are referred to as phases of mood elevation, they may involve concurrent dysphoria, particularly with distressing anxiety symptoms. Anxiety and irritability occur commonly in bipolar depression. Suicide is a greater risk during depression when there is associated anxiety. Comorbid anxiety disorders, such as panic disorder and generalised anxiety disorder, are common in bipolar disorder.

### Substance misuse

Bipolar illnesses are often complicated by use of alcohol or illicit drugs. Substance misuse is more common in bipolar I disorder (50%) than bipolar II disorder (39%); alcohol is the most commonly misused substance (42% and 34% for bipolar I and II, respectively),<sup>3</sup> and illicit drug use is also common. Sometimes the mood disorder will be undiagnosed in the context of florid substance misuse. Diagnosis can be problematic in such patients because alcohol and many drugs can cause substantive mood alterations that remit without treatment once substance use ceases.

### Common diagnostic challenges

Differentiation of bipolar disorders from schizophrenia may be difficult, especially in young people with short medical histories. Severe bipolar depression may present as catatonia, and mania with psychosis may present as catatonic excitement. Substance misuse may contribute to mood swings that resolve on drug withdrawal. Unipolar depression, or recurrent unipolar depressions, which may be treatment resistant, can be present before mania or hypomania are apparent. Attention deficit hyperactivity disorder may be misdiagnosed as hypomania. The mood swings with borderline personality disorder may be misdiagnosed as bipolar disorder, but this is a challenging issue as borderline personality disorder and bipolar disorder may coexist.

### Frequency of mood changes

Most patients with bipolar disorder will have two or fewer episodes of mood disorder per year. Some may have many years between episodes. In this latter case, when there is an episode of bipolar mood elevation or depression after many years of euthymia, the clinician should always check for possible organic precipitants. Patients who have four or more episodes in one year are referred to as having a rapid cycling disorder. These patients are typically difficult to treat and often unresponsive to conventional mood stabiliser regimens (see Malhi et al, *page S24*).<sup>12</sup> Occasionally, patients may experience mood changes more than once per day, typically being depressed in the morning, with mood elevation in the evening or at night. This has been referred to as

### 4 Guide for diagnosing a hypomanic episode\*

- A. A distinct period of persistently elevated, expansive or irritable mood, lasting throughout at least 4 days.
- B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and are significant:
  - (1) inflated self-esteem or grandiosity
  - (2) decreased need for sleep
  - (3) more talkative than usual
  - (4) flight of ideas or feeling that thoughts are racing
  - (5) distractibility
  - (6) increase in goal-directed activity, or agitation
  - (7) excessive involvement in pleasurable but high-risk activities (eg, buying sprees, sexual indiscretions or foolish investments).
- C. The episode is associated with an unequivocal change in functioning, uncharacteristic of the person.
- D. The disturbance in mood and the change in functioning are observable by others.
- E. The episode is not severe enough to cause marked impairment or necessitate hospitalisation, and there is no psychosis.
- F. The symptoms are not due to the direct physiological effects of a drug of misuse or medication, or a general medical condition (eg, hyperthyroidism).

\* Derived from the *Diagnostic and statistical manual of mental disorders*, fourth edition, text revision.<sup>1</sup>

ultradian cycling, and can raise diagnostic confusion with borderline personality disorder.

### Neurological changes in bipolar disorder

Consistent with a prevailing view that bipolar disorder has a primary biological basis, structural neuroimaging studies have revealed a reduction in central nervous system volume in patients with bipolar I disorder and increased rates of deep white matter hyperintensities.<sup>13</sup> There may be a loss of hippocampal volume, consistent with that seen in untreated depression.<sup>14,15</sup> There are also significant cognitive deficits in bipolar disorder, even during euthymia, which can impede functioning.<sup>16</sup> These impairments can result in patients who seem to have achieved symptomatic recovery not regaining full social and occupational rehabilitation. Thus, a goal of treatment should be a full remission of all symptoms and rehabilitation, rather than only alleviation of mood symptoms.<sup>16</sup>

### Progress of illness

Antecedent depression may predate the first episode of mood elevation by many years. Mood elevation may seem to be the element which defines bipolar disorder, but depression is the more enduring element of the illness and results in the greatest disability over time.<sup>17</sup>

There is controversy over the long-term outcome of bipolar depression. Clinically, some experts believe that depressive episodes tend to become more severe over time, while mood elevation tends to decline over time. However, some data suggest that the proportions of mania and depression remain stable into old age.<sup>18</sup> Depression is not always full syndromic major depression. Even less severe depressive states can cause considerable disability,

demoralisation, and increase the likelihood of a more complete relapse that may result in hospitalisation.

Treatment progress tends to be hindered by substance misuse, repeated relapses, gaps in pharmacotherapy and psychosocial disruptions. Prognosis appears to be better for patients in continued treatment that includes pharmacotherapy, psychological and social interventions, exercise, social rhythm therapy, and effective work and social rehabilitation.

## Conclusion

Diagnosis of bipolar disorder requires at least one episode of mood elevation, either mania or hypomania. However, the dominant and most disabling phase of this illness is depression. Establishing the correct diagnosis is important as the prognosis is different to that for major depressive disorder, and treatments are generally different. Diagnosis may not be possible on first presentation of depression, but only made after a subsequent mood elevation. Clinicians should review diagnoses regularly, and remain open to bipolar diagnoses as it is possible to confuse these with major depressive disorder, schizophrenia and substance misuse. Corollaries of effective diagnosis are an informed patient and appropriate treatments, with the potential for better outcomes.

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