Bipolar disorder – diagnosis and current treatment options

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Bipolar disorder is a complex condition characterised by both manic and depressive episodes. Here the authors discuss the challenges faced in both diagnosis and treatment.

**KEY POINTS**

- misdiagnosis as unipolar depression, personality disorder, a primary drug or alcohol problem or even schizophrenia is a common problem
- it is important that GPs develop awareness and competencies in the assessment, diagnosis and treatment of bipolar disorder
- few primary-care clinicians make use of available screening instruments for hypomania – the BSDS may be particularly useful for identifying hypomania
- cardinal symptoms of mania include elevated mood, flight of ideas, pressure of speech, increased energy levels, reduced need for sleep and increased activity levels
- antidepressants may be of limited therapeutic benefit in the treatment of bipolar depression and may cause destabilisation of mood in some patients
- treatment with lamotrigine or quetiapine is recommended by the BAP
- most patients with mania will require short-term pharmacological treatment in an appropriate clinical setting
- valproate or an atypical antipsychotic has a rapid antimanic effect and can be started in severely unwell manic patients not already on treatment
- long-term treatment of bipolar disorder should be started after a single severe manic episode – lithium monotherapy should be considered as an initial treatment
- long-term combination treatment is recommended when monotherapy fails or subthreshold affective symptoms are ongoing

**Epidemiology and diagnostic challenges**

Bipolar disorder type I affects around 1 per cent of the population and type II disorder affects a further 2–3 per cent. The disorder is a significant cause of disability and suffering. A recent international study reported that the median age at onset is 24 years for men and 27 years for women with a range of 10 to 42 years, although most individuals with bipolar disorder report problems with mood and anxiety symptoms in adolescence and early adulthood.

Bipolar I and II and bipolar spectrum disorders can pose significant diagnostic challenges. Many bipolar I and II patients will experience a delay of several years between the onset of significant manic symptoms and receiving the correct diagnosis. Misdiagnosis as unipolar depression, personality disorder, a primary drug or alcohol problem or even schizophrenia is a common problem that has been linked to poorer long-term outcomes.

Despite significant interindividual variation, most patients with bipolar disorder suffer a predominance of depressive symptoms during their lifetime.

Bipolar disorder is a common, chronic and highly morbid mental illness characterised by manic and depressive episodes that often run a relapsing and remitting course (see Table 1). The key feature differentiating bipolar disorder from recurrent depressive disorder is a lifetime presence of mania, hypomania or mixed affective episodes.

The Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV) distinguishes between bipolar I disorder, where mania occurs, and bipolar II disorder, where hypomania occurs usually alongside one or more episodes of major depression.
Although the majority of psychiatric care for patients suffering with bipolar disorder is delivered by local community mental health teams, the level of these services varies across the UK. It is therefore important that GPs develop awareness and competencies in the assessment, diagnosis and treatment of bipolar disorder.

Screening instruments for the detection of depression in primary care such as the Patient Health Questionnaire (PHQ), the Hospital Anxiety and Depression Scale (HADS) and the Beck Depression Inventory (BDI) are routinely used but very few primary-care clinicians make use of available screening instruments for hypomania.

Relevant screening tools for hypomania include as the Mood Disorder Questionnaire (MDQ), the Bipolar Spectrum Diagnostic Scale (BSDS), and the Hypomania Checklist (HCL-32). All of these instruments are relatively brief and have been validated for use in a range of clinical settings. The BSDS may be particularly useful for identifying hypomania in primary-care patients with depression. 7

Causes
There is a significant association between the risk of development of bipolar disorder and a family history of affective disorder, in particular bipolar affective disorder.

Although the majority of patients with bipolar disorder have no family history of the condition, genetic risk has long been identified as an important factor in identifying at-risk individuals. A 2009 population-based study found there to be a relative risk of 6.4 for children of bipolar patients and 7.9 for siblings of bipolar patients. The total heritability for the disorder was calculated as 59 per cent. 11

Many candidate gene association studies have been carried out but results have generally been inconsistent. There is currently no consensus on robust candidate genes for bipolar disorder. It is likely that many genes, each of small effect, will be implicated.

Environmental risk factors are also important aetiologically. A 2003 systematic review found that noncaucasian ethnicity, pregnancy and obstetric complications, lower premorbid IQ, poor premorbid adjustment, early parental loss, seizure disorder and childbirth are all associated with the development of bipolar disorder. 12

Signs and symptoms
Manic episodes may be preceded by a prodrome, which can last from a few days to a few months, of mild and often transitory and indistinct manic symptoms. At times, however, no prodromal warning signs occur and the episode can start abruptly.

The cardinal symptoms of mania include elevated mood (this can include irritability or euphoria), flight of ideas, pressure of speech, increased energy levels, reduced need for sleep and increased activity levels. These symptoms can be exaggerated and accompanied by delusions (often mood congruent) in more severe manic episodes. Psychotic symptoms in mania are often florid and bizarre and most episodes of mania last from several weeks to around three months in duration. 13

Depressive episodes in bipolar disorder may have a relatively abrupt onset and include several atypical features. Sufferers of bipolar depression display higher rates of psychotic symptoms compared with their unipolar depressed counterparts. Furthermore they report increased rates of irritability, discontented mood and profound anergia. 3 If untreated, episodes of bipolar depression can persist for many months.

Management of bipolar disorder
One of the most important practical issues in the management of diagnosed or suspected bipolar disorder is the use of antidepressants.

Recent evidence suggests that antidepressants may be of limited therapeutic benefit in the treatment of bipolar depression and may for a proportion of patients be unhelpful by causing destabilisation of mood (particularly with tricyclic antidepressants and venlafaxine14), more frequent mood episodes, treatment resistance and possibly also (especially bipolar I disorder)

Characterised by at least one manic episode or mixed affective episode (clear manic and depressive features present in the same episode). There is almost always a history of depressive episodes, although these are not necessary for establishing a diagnosis.

Bipolar II disorder
Characterised by one or more major depressive episodes, together with at least one hypomanic episode in the clinical course.

Table 1. Definition of bipolar I and bipolar II disorder according to the American Psychiatric Association (1994)
in young bipolar patients) an increase in suicidal behaviour. 7

It may be prudent to avoid antidepressant monotherapy in patients with bipolar depression who have previously found antidepressants unhelpful – either due to lack of efficacy or adverse effects. Treatment with lamotrigine or quetiapine is recommended by the British Association for Psychopharmacology (BAP).

Acute mania or mixed affective state
Most patients with mania will require short-term pharmacological treatment in an appropriate clinical setting. No psychotherapy currently provides an alternative strategy for management. A less noisy and stimulating environment with higher nursing staff-patient ratios may reduce behavioural disturbance in some patients with mania. 14

Valproate or an atypical antipsychotic has a rapid antimanic effect and can be started in severely unwell manic patients not already on treatment for bipolar disorder. Asenapine (Sycrest) is also used in the acute treatment of manic or mixed episodes of bipolar I disorder. Recent evidence indicates that this agent is well tolerated and may also be suitable for longer-term maintenance therapy of bipolar I disorder. 15

For less unwell manic patients lithium or carbamazepine may also be considered as a short-term treatment. Short-term adjunctive sedative treatment with a benzodiazepine such as
diazepam or clonazepam can also be helpful. Antidepressant therapy should be tapered and discontinued. Treatment, where possible, should be guided by patient preference.14

Bipolar depression
Quetiapine should be considered where an early response to treatment is desired for patients who suffer an acute episode of bipolar depression and who are not already on long-term treatment for bipolar disorder. Lamotrigine with an appropriate dose titration should also be considered. These medications should be considered closely when there is evidence that previous antidepressant treatment has caused a change in mood polarity.14

Antidepressant treatment (typically an SSRI) with an antimanic agent (eg lithium, valproate or an antipsychotic) may be considered for depressed patients with no prior history of mania. Antidepressant monotherapy is not recommended in patients who have previously been manic due to an increased risk of switch into mania. Although not absolutely contraindicated, antidepressants should be used with caution in patients with a history of hypomania and usually alongside mood stabiliser cover.

Tricyclic antidepressants and other dual reuptake inhibitor agents such as venlafaxine – and possibly duloxetine (Cymbalta) – carry a greater risk of precipitating a switch into mania than other antidepressants and are not recommended except for patients who fail to respond to an initial treatment.

Slow, tapered antidepressant discontinuation (preferably within three months of resolution of a depressive episode14) can be considered following appropriate response to treatment.14

Antipsychotic medication should be considered in the presence of psychotic symptoms,14 and electroconvulsive therapy should be considered for patients with high suicidal risk, psychosis, severe depression during pregnancy or life-threatening features of depression. When depressive symptoms are less severe, lithium or possibly valproate may be considered (although valproate should not generally be prescribed for women of child-bearing potential due to risks of teratogenicity).14

Interpersonal therapy, cognitive behaviour therapy or family-focused therapy (FFT) are also useful as there is evidence that these therapies can shorten an episode of bipolar depression.14

Relapse prevention
Long-term treatment of bipolar disorder should be started after a single severe manic episode; although there is no controlled evidence, early recognition and treatment of bipolar disorder may lead to a more benign illness course. Long-term pharmacological treatment should be alongside appropriate psychological and social support.14

Lithium monotherapy should be considered as an initial treatment as it is probably effective against both manic and depressive relapse, although it is more effective in preventing mania.14 Due to possible toxicity serum lithium concentration monitoring is required. Patients often carry a lithium alert card due to this possibility (see Figure 1). If lithium is ineffective or poorly tolerated there are a number of alternatives recommended by the BAP (see Table 2).

If lithium or one of the medications listed in Table 2 is effective in achieving remission from a depressive or manic episode it should be considered for long-term relapse prevention.14

Long-term combination treatment is recommended when monotherapy fails or subthreshold affective symptoms are ongoing.

Table 2. Alternatives to lithium for relapse prevention in bipolar disorder14

- aripiprazole prevents manic relapse
- carbamazepine is less effective than lithium but may sometimes be employed as monotherapy if lithium is ineffective and especially in patients who do not show the classical pattern of episodic euphoric mania; pharmacokinetic interactions are a particular problem for carbamazepine and caution is advised
- oxcarbazepine may be considered by extrapolation because of its lower potential for such interactions
- lamotrigine prevents depressive more than manic relapse
- olanzapine prevents manic more than depressive relapse
- quetiapine prevents both manic and depressive relapse
- valproate probably prevents both manic and depressive relapse

Figure 1. Patients receiving lithium therapy often carry an alert card due to possible toxicity

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When a patient experiences predominantly manic relapses it may be logical to combine predominantly antimanic agents (e.g., lithium, valproate or an antipsychotic). When a patient experiences predominantly depressive symptoms, lamotrigine or quetiapine may be more appropriate. Long-term antidepressant treatment should be used with caution where indicated.

**Psychoeducation for bipolar disorder**

Despite significant benefits of medication in bipolar disorder, poor insight and medication adherence can lead to reduced long-term outcomes for bipolar disorder.

There is evidence that psychoeducational interventions are effective in bipolar disorder with particular benefits in relapse rates and medication adherence. Availability of psychoeducational interventions for bipolar disorder is increasing with particular emphasis on online psychoeducational packages (www.bep-c.org).

**Conclusion**

Bipolar disorder is a complex disorder of mood and behaviour that requires a multimodal treatment and diagnostic approach. Particular attention should be given to the early features of the condition, heterogeneity of presentations, relapse prevention and evolving therapies for the condition.

**References**


**Declaration of interests**

None to declare.

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