Proving that a patient has bipolar disorder

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Abstract

Bipolar disorder (BPD) is commonly misdiagnosed; this article concisely outlines the sub-types of BPD, important criteria essential for diagnosis and then demonstrates the most effective method of extracting the necessary information. Using the twenty-nine questions provided, health professionals can be confident they have checked sufficiently for symptomatology that is often missed; this should help to confirm whether a patient has BPD. The aim should remain to reduce morbidity and mortality due to misdiagnosis, by improving the sensitivity of screening, enabling faster access to the correct treatment for these vulnerable patients.

Key words: bipolar disorder, diagnosis

Introduction

Bipolar disorder (BPD) is a recurrent, cyclical disorder that combines opposite, but related, mood states, including depression, mania or hypomania and mixed states. It is further differentiated into sub-syndromes (bipolar I and II). Current diagnostic criteria using the DSM-IV for BPD type-I requires the occurrence of one or more manic episodes or mixed episodes. Patients may also have one or more depressive episodes. Importantly, in the period between these episodes, most patients return to their normal state of wellbeing. Bipolar II disorder is characterised by at least one hypomanic episode as well as one or more major depressive episodes.

Epidemiological studies have indicated that the lifetime prevalence is 1% across all populations. However, additional studies (1) have suggested that BPD is more common than originally thought. This is due to the recognition that BPD has a spectrum of expression, resulting in sub-threshold BPD, not completely fulfilling DSM criteria (2), being under-detected.

The importance of diagnosing bipolar disorders correctly could play a role in the public health challenge of reducing the associated premature mortality due to suicide (3-4). Furthermore, the comorbidity of BPD often includes anxiety disorders and substance abuse. It has been suggested that substance abuse in bipolar disorder represents unregulated self-medication by these patients (5).

In this article, we discuss an effective method of diagnosing BPD in clinical practice that has been developed for use in patients who have been referred to secondary care in a euthymic state. Diagnosis is often obscured by uncertainties. Asking: "Do you get moods which go up and down?" is simply not enough.

Management of BPD requires long-term treatments, mood stabilisers, which have important, often life-changing adverse effects. Increased suicidality in BPD means that it is essential that the diagnosis is confirmed and that the correct, effective treatment is provided.

Classification of BPD
Definition of Hypomania subtypes

ICD 1013	DSM-IV2
Two episodes of Mood Disturbance	One episode of mood disturbance
Hypomania & Mania Distinct	Describes degrees of Mania
Single entity of BPD	Bipolar I – Mania Bipolar II – Hypomania
Different classifications for present state	Different classifications for present state

	Threshold (DSM-IV)2	Subthreshold (DSM-V)
Severity	Stem criteria:	
	Elevated/irritable mood	Elevated/irritable mood OR over-reactive
	+ 3-4 hym sx	+ 2 or more hym sx
Duration	4 days minimum	2 or more days

Detection, Misdiagnosis & Screening

The first symptom of BPD in ~50% of patients is depression (6). Long-term follow-up studies (12.8 years) conducted by Judd et al. (7) found patients with BPD were symptomatic, (depressed, manic, hypomanic or in a mixed state) approximately 47% of their lives.

Misdiagnosis is, however, a very common problem. The Depressive and Bipolar Support Alliance (DBSA) found that large-scale retrospective studies (8) indicated the most frequent misdiagnosis was unipolar depression, and also that >35% of misdiagnosed patients reported experiencing BPD symptomatology ~10years prior to BPD diagnosis (9). These findings are supported by Ghaemi et al. (10) who showed patients wait 9 years, on average, for a BPD diagnosis.

Hirschfield et al. (9) showed that the Mood Disorder Questionnaire (MDQ) overall positive screen rate, for BPD, was 3.7% (when adjusted for non-response bias) across a population of 83,358 US citizens (>18yrs). Of those for whom the MDQ suggested BPD, only 19.8% had previously received a diagnosis from a physician, 31.2% had a unipolar depression diagnosis, and 49.0% had no BPD or unipolar diagnosis. Positive screens were highest amongst young adults from lower socio-economic areas in this study. These patients were also significantly more likely to suffer from migraine and asthma. Substance misuse was also higher in this cohort.

BPD – Subtypes or Spectrum?

The spectrum concept of BPD was first proposed in 1977 when a prospective study showed that people with cyclothymic mood disorder go on to develop unipolar depression (UPD) or BPD (11). Another showed that 12% of patients in the study went on to develop BPD type II; having had a UPD diagnosis 15 years earlier (12).

Sub-threshold bipolar patients have also been seen to progress towards BPD, one study indicating a progression of 7% of such patients with BPD type II advancing to BPD type I, over 15years (14).

The Importance of Bipolar II

Hypomania often goes undiagnosed, due to the reduced impact on the patient's life. These patients tend to present in a euthymic condition or when experiencing depressive symptoms. Often a history of hypomania may be missed, or BPD type II (mixed state) may be misdiagnosed as an agitated depression (15). This poses a very real risk to patients; undiagnosed patients with BPD may progress to manic/hypomanic or mixed states as a result of treatment with antidepressants, in particular venlafaxine. This dramatically increases suicide risk in these patients (16).

Bipolar markers in major depressive episode (8, 17)	
Historical Markers	Cross-Sectional Markers
FH of Bipolar I/II disorder (suicide) Past hypomania (≥ 2 days, incl. Iatrogenic)** > 3 depressive episodes Seasonal onset (Winter ≈ BPD II, Summer ≈ BPD I) Panic attacks, GAD,OCD/OC symptoms** Cyclothymia hyperthymia**	Retardation* Psychotic features* Catatonic features* Early onset Atypical features** Depressive mixed states/agitated depression** Panic attacks/disorder, 2 or more anx. disord.**

Figure 1 *Mostly BPD Type I, ** Mostly BPD Type II
(After Akiskal and Bennazi, Clin Appr Bipol Disord 2003, 2: 41-47 & Benazzi and Rihmer, Psych. Res. 2000, 93: 257-262.)

Summary

- BPD is under-referred, under-diagnosed & under-treated leading to iatrogenic effects , in turn leading to increased negative side effects e.g. substance misuse, suicide.
- Prevalence of BPD, including threshold & sub-threshold Type II, may be higher than previously thought.
- BPD Type II is much more common than Type I
- Therefore accurate diagnosis is important for effective treatment.

"Is my patient bipolar?"

We have developed a method for assessing patients referred in a euthymic state by their GP, to secondary care, in order to ascertain whether they have BPD. The mood disorder is investigated in the following order.

- High moods: intensity & frequency.
- Depressive moods.
- Mixed states.
- Disorders often associated with BPD.
- Family history.
- Substance abuse.
- Current depressive episode.

The questions asked will be presented in bold print and beneath them is given in normal print the rationale for the question.

Q.1 You are aware of how it feels when you are depressed. How old were you when you had your first depressive episode (treated or untreated)?
From experience, we often find patients report a primary depressive episode during their early to mid-teenage years. This is supported by research which has shown:

- BPD is known to be diagnosed on average 6 years prior to UPD (unipolar depression) (18).
- BPD diagnoses may take ~10years after onset BPD symptomatology (9).

Q.2 After that, did you proceed to suffer recurrent depressive episodes?
Patients with recurrent depressive disorder may develop BPD Type II over time (7,14).

Q.3 Looking back, when was your first hypomanic episode?
UPD has been proven occasionally to develop over time into BPD type II with the first episode of hypomania (14).

Q.4 How long do the hypomanic episodes last?
The DSM Criteria (2) suggest 4 days is diagnostic; and 2 days would be sub-syndromal. However, on investigation, often patients say that they are aware of a day when there is an upward shift in their mood, prior to full mania/hypomania, and another day where their mood is returning to their prior state.

Q.5 When you are high, hypomanic, do you find:

- You need less sleep?
- Experience racing thoughts?
- Talk quickly and hop from one though to another?
- Spend excessively perhaps accruing debt?
- Find you mix with lots of new people, or are more flirtatious than usual?
- Take more risks than usual?

In order to validate the responses to these questions PHQ-919 and GAD-720 can usually also be administered at this point.

Q.6 When you are depressed do you find you comfort eat?
This is common, as atypical depression is linked with BPD (21).

Q.7 When you are depressed do you find you sleep a lot during the day?
Also common as atypical depression is linked with BPD (20).

Q.8 When you are depressed can you concentrate?
Patients often experience difficulties with concentration and attention span when depressed (2).

Q.9 When you are depressed, can you enjoy things?
Patients often experience anhedonia when depressed (2).

Q.10 How long do your periods of depression last?
Often weeks or months; in BPD low moods last longer than high moods However, evidence suggests episodes of unipolar depression last longer (21).

Q.11 When you are depressed, do you get suicidal thoughts?
In practice, patients are often forthcoming about their thoughts; suicidal ideation is a common aspect of BPD (2).

Q.12 When you are depressed, do you ever get severe retardation (being slowed down), paranoia, or have hallucinations.
Psychotic depression, including catatonia may be a concomitant of bipolar disorder (2).

Q.13 Do you often get irritable or angry?
This is a common feature; often such irritability is linked with a mixed state15.
Q.14 Does it sometimes happen that your mood changes rapidly from high to low within a day?
These mixed affective episodes are one subtype of mixed affective state15.

Q.15 Do you sometimes find that you are happy and crying at the same time?
Dysphoric mania is a form of mixed affective state16.

Q.16 Do you sometimes find that you are depressed and very irritable at the same time?
Agitated Depression is a form of mixed affective state16.

Q.17 When you are in a mixed state, as we have just described, do you often find that you have marked suicidal ideation?
Patients are more likely to commit suicide when in a mixed state, and thus experience greater suicidal ideation16.

Q.18 In one year, do you get 4 or more changes of mood; at least 2 highs and 2 lows?

Often patients find this to be the case, and it implies rapid cycling. Rapid cycling patients are more difficult to treat and have increased suicidality10.

Q.19 Do you suffer from migraine?
There are genetic links between BPD and migraine, so this may increase likelihood that BPD is the cause9.

Q.20 Do you suffer with anxiety or panic disorder?
Comorbid anxiety disorders are common in bipolar disorder20.

Q.21 Do you suffer from OCD symptoms?
OCD is often linked with BPD and such patients are particularly difficult to treat with medication1.

Q.22 You may have been told that you have 'borderline' symptoms but do you also have episodes of HIGH mood, lasting >4 days?
Borderline personality disorder patients have mood 'swings' from low to normal - not high2. Therefore if they have high moods they are comorbid borderline/bipolar.

Q.23 Do you suffer from irritable bowel syndrome (IBS) or colitis?
This is another common co-morbidity. There may be immunological links, in association with levels of inflammation, between these conditions and BPD1.

Q.24 Do you suffer muscular tension?
This is another common co-morbidity2.

Q.25 Do you have a family history of BPD, suicide, or psychosis?
Patients often report that a family member spent periods of time as an inpatient, or that their relative suffered with depression. However, they are often unaware of the concept of mania.

Q.26 Do you drink alcohol to excess?
Many persons who suffer from depression use alcohol. Alcohol is a depressant. On the other hand there may be other causes of the depression. Other substances such as cocaine cause euphoria and depression when withdrawn. Cannabis has many effects on mood, often complicating diagnosis5.

Q.27 Do you find episodes of high/low mood are particularly associated with different seasons?
BPD Type I is worst in summer, and BPD Type II is worst in winter22.

Q.28 Do you think of yourself as creative?
Patients with BPD are often very creative individuals.

Q.29 Have antidepressants ever caused your mood to become high?
BPD often presents with mania/hypomania caused by antidepressants: BPD type III (iatrogenic) (15).

It is important to ascertain whether the patient is depressed at the present time. This should be investigated by repeating questions related to depression in the present tense and validating these responses using the PHQ9 and GAD7. It is important at this stage to investigate any current suicidal ideation and planning. Once all these questions have been asked, all the information needed to diagnose BPD will be available. The whole interview should take <60 minutes to complete.

We believe that every patient who is suspected of having bipolar disorder or who suffers from depression, recurrent depression, and 'depression with anxiety' should be evaluated as above. The details of the answers to these questions should be recorded in notes, the letter to the GP, or in the ward discharge summary. A mood stabiliser is required for patients diagnosed with BPD; this will be a life-long treatment, and may have adverse effects that will need to be monitored and managed.

Patients with BPD should only be treated with antidepressants while depressed (15). Specific drugs are effective in bipolar depression e.g. quetiapine, lamotrigine. Patients with BPD are often initially considered to have treatment-resistant depression; however, antidepressants may induce rapid cycling or increase the incidence of mixed states, increasing the risk of suicide.
It is important to engage the patient in treatment, by giving them literature about the mood-stabilisers and their adverse effects in a clear format, as found in patient-friendly websites. The clinician should meet with the patient again after one week, once they have had sufficient time to weigh the benefits and adverse effects of the proposed medication, with the aim of allowing them to come to an informed decision.

When patients with BPD are receiving antidepressants for a depressive phase, they should be seen every 2-3 weeks so that the antidepressant medication can be stopped once their mood has improved. This is in line with current guidelines for BPD, in order to prevent inducing mania (15). Patients experiencing mixed states, due to their increased risk of suicide, should be assigned a care co-ordinator and then be followed up by the crisis team or Community Mental Health Team. When experiencing mixed states it is important to stop antidepressants, as previously mentioned, increase the mood stabilizer (if possible), and start an atypical antipsychotic if they are not on one already15.

In conclusion, BPD is an unpleasant disorder, the treatment of which is complicated and still imperfect. By following these guidelines, we believe that misdiagnosis can be reduced, quality of life can be improved and, because suicide risk is likely to be increased with poor management, that some lives can even be saved. It is vital that appropriate follow up and monitoring is in place to protect these very vulnerable patients.

GP Comment

What have I learned from this paper?

This article reinforces the importance of avoiding the incorrect diagnosis of unipolar depression in patients with bipolar disorder, if they are to be treated effectively and safely. The authors present a series of useful questions that can be used to assess carefully for a previous history of mania/hypomania and for clinical features that increase the likelihood that the correct diagnosis is bipolar disorder.

Dr Jenny Hopwood, GP trainee.

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